

## Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSSPTA1626GMS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS 1 DEC 01 Web Page for STN Seminar Schedule - N. America  
NEWS 2 DEC 01 ChemPort single article sales feature unavailable  
NEWS 3 APR 03 CAS coverage of exemplified prophetic substances enhanced  
NEWS 4 APR 07 STN is raising the limits on saved answers  
NEWS 5 APR 24 CA/Cplus now has more comprehensive patent assignee information  
NEWS 6 APR 26 USPATFULL and USPAT2 enhanced with patent assignment/reassignment information  
NEWS 7 APR 28 CAS patent authority coverage expanded  
NEWS 8 APR 28 ENCOMPPLIT/ENCOMPPLIT2 search fields enhanced  
NEWS 9 APR 28 Limits doubled for structure searching in CAS REGISTRY  
NEWS 10 MAY 08 STN Express, Version 8.4, now available  
NEWS 11 MAY 11 STN on the Web enhanced  
NEWS 12 MAY 11 BEILSTEIN substance information now available on STN Easy  
NEWS 13 MAY 14 DGENE, PCTGEN and USGENE enhanced with increased limits for exact sequence match searches and introduction of free HIT display format  
NEWS 14 MAY 15 INPADOCDB and INPAFAMDB enhanced with Chinese legal status data  
NEWS 15 MAY 28 CAS databases on STN enhanced with NANO super role in records back to 1992  
NEWS 16 JUN 01 CAS REGISTRY Source of Registration (SR) searching enhanced on STN  
NEWS 17 JUN 26 NUTRACEUT and PHARMAML no longer updated  
NEWS 18 JUN 29 IMSCOPROFILE now reloaded monthly  
NEWS 19 JUN 29 EPFULL adds Simultaneous Left and Right Truncation (SLART) to AB, MCLM, and TI fields  
NEWS 20 JUL 09 PATDPAFULL adds Simultaneous Left and Right Truncation (SLART) to AB, CLM, MCIM, and TI fields

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4,  
AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009

NEWS HOURS      STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN      Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 11:25:28 ON 13 JUL 2009

==>

## Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

## => FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.22	0.22

FILE 'REGISTRY' ENTERED AT 11:25:50 ON 13 JUL 2009  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1  
DICTIONARY FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1

New CAS Information Use Policies. enter HELP USAGETERMS for details.

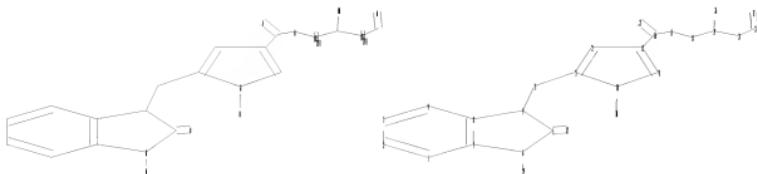
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=> Uploading C:\Program Files\Stnexp\Queries\10580670.str



chain nodes :

15 16 17 18 19 20 21 22 23 26 29 30 31

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

5-22 6-29 9-15 10-30 11-15 13-16 16-17 16-23 17-18 18-19 19-20 19-26

20-21 21-31

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :

5-6 5-22 6-7 10-11 10-14 16-17 16-23 19-26 21-31

exact bonds :

5-9 6-29 8-9 9-15 10-30 11-12 11-15 12-13 13-14 13-16 13-18 17-18 18-19 19-20  
20-21

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8

isolated ring systems :

containing 1 : 10 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 26:CLASS 29:CLASS 30:CLASS

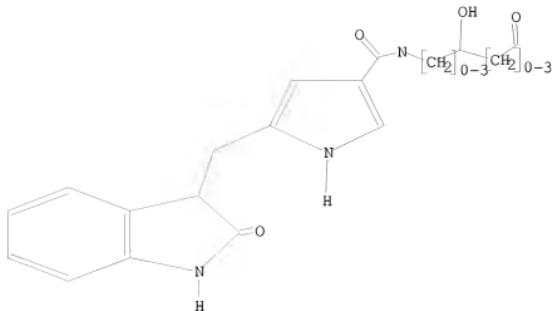
31:CLASS

L1 STRUCTURE UPLOADED

=&gt; d 11

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s 11
SAMPLE SEARCH INITIATED 11:26:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -          0 TO ITERATE

100.0% PROCESSED      0 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:      0 TO      0
PROJECTED ANSWERS:         0 TO      0

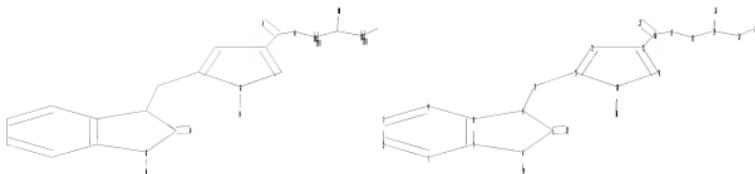
L2      0 SEA SSS SAM L1

=> s 11 sss full
FULL SEARCH INITIATED 11:26:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -          0 TO ITERATE

100.0% PROCESSED      0 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01

L3      0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10580670a.str
```



chain nodes :

15 16 17 18 19 20 21 22 23 26 29 30

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

5-22 6-29 9-15 10-30 11-15 13-16 16-17 16-23 17-18 18-19 19-20 19-26

20-21

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :

5-6 5-22 6-7 10-11 10-14 16-17 16-23 19-26

exact bonds :

5-9 6-29 8-9 9-15 10-30 11-12 11-15 12-13 13-14 13-16 13-18 17-18 18-19 19-20  
20-21

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8

isolated ring systems :

containing 1 : 10 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS

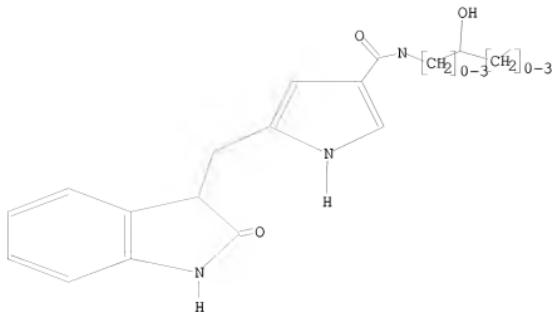
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 26:CLASS 29:CLASS 30:CLASS

L4 STRUCTURE UPLOADED

=&gt; d 14

L4 HAS NO ANSWERS

L4 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s 14
SAMPLE SEARCH INITIATED 11:28:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -          0 TO ITERATE

100.0% PROCESSED      0 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:      0 TO      0
PROJECTED ANSWERS:         0 TO      0

L5      0 SEA SSS SAM L4

=> s 14 sss full
FULL SEARCH INITIATED 11:29:05 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -          0 TO ITERATE

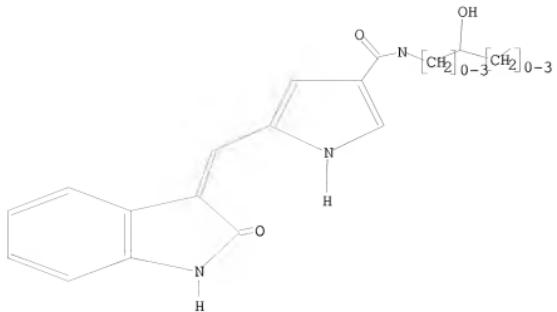
100.0% PROCESSED      0 ITERATIONS          0 ANSWERS
SEARCH TIME: 00.00.01

L6      0 SEA SSS FUL L4

=>
Uploading C:\Program Files\Stnexp\Queries\10580670b.str
```

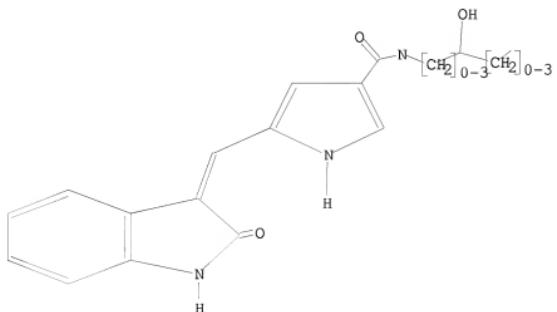


10580670



Structure attributes must be viewed using STN Express query preparation.

=> d 17  
L7 HAS NO ANSWERS  
L7 STR



Structure attributes must be viewed using STN Express query preparation.

=> s 17  
SAMPLE SEARCH INITIATED 11:30:46 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 66 TO ITERATE

100.0% PROCESSED 66 ITERATIONS 46 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*  
 PROJECTED ITERATIONS: 833 TO 1807  
 PROJECTED ANSWERS: 514 TO 1326

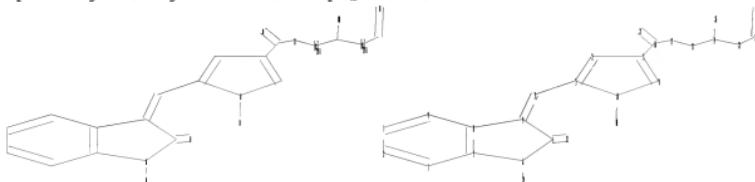
L8 46 SEA SSS SAM L7

=> s 18 sss full  
 FULL SEARCH INITIATED 11:30:59 FILE 'REGISTRY'  
 FULL SCREEN SEARCH COMPLETED - 1271 TO ITERATE

100.0% PROCESSED 1271 ITERATIONS 853 ANSWERS  
 SEARCH TIME: 00.00.01

L9 853 SEA SSS FUL L7

=>  
 Uploading C:\Program Files\Stnexp\Queries\10580670d.str



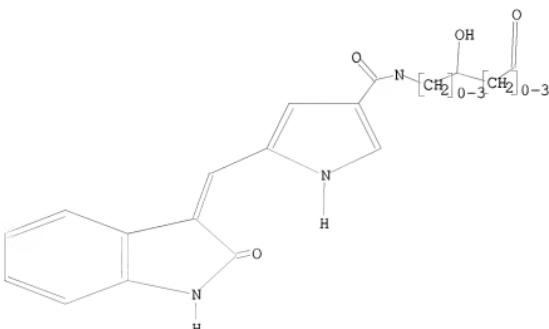
chain nodes :  
 15 16 17 18 19 20 21 22 23 26 29 30 32  
 ring nodes :  
 1 2 3 4 5 6 7 8 9 10 11 12 13 14  
 chain bonds :  
 5-22 6-29 9-15 10-30 11-15 13-16 16-17 16-23 17-18 18-19 19-20 19-26  
 20-21 21-32  
 ring bonds :  
 1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14  
 exact/norm bonds :  
 5-6 5-22 6-7 10-11 10-14 16-17 16-23 19-26 21-32  
 exact bonds :  
 5-9 6-29 8-9 9-15 10-30 11-12 11-15 12-13 13-14 13-16 17-18 18-19 19-20  
 20-21  
 normalized bonds :  
 1-2 1-7 2-3 3-4 4-8 7-8  
 isolated ring systems :  
 containing 1 : 10 :

10580670

Match level :  
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS  
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 26:CLASS 29:CLASS 30:CLASS  
32:CLASS

L10 STRUCTURE UPLOADED

=> d l10  
L10 HAS NO ANSWERS  
L10 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l10  
SAMPLE SEARCH INITIATED 11:32:28 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 58 TO ITERATE

100.0% PROCESSED 58 ITERATIONS 34 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 704 TO 1616  
PROJECTED ANSWERS: 331 TO 1029

L11 34 SEA SSS SAM L10

=> s l10 sss full  
FULL SEARCH INITIATED 11:32:34 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1068 TO ITERATE

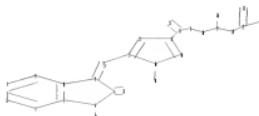
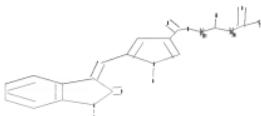
10580670

100.0% PROCESSED 1068 ITERATIONS  
SEARCH TIME: 00.00.01

520 ANSWERS

L12 520 SEA SSS FUL L10

=>  
Uploading C:\Program Files\Stnexp\Queries\10580670x.str



chain nodes :

15 16 17 18 19 20 21 22 23 26 29 30 32 34

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

5-22 6-29 9-15 10-30 11-15 13-16 16-17 16-23 17-18 18-19 19-20 19-26  
20-21 21-32 21-34

ring bonds :

1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :

5-6 5-22 6-7 10-11 10-14 16-17 16-23 19-26 21-32 21-34

exact bonds :

5-9 6-29 8-9 9-15 10-30 11-12 11-15 12-13 13-14 13-16 17-18 18-19 19-20  
20-21

normalized bonds :

1-2 1-7 2-3 3-4 4-8 7-8

isolated ring systems :

containing 1 : 10 :

G1:CH,NH2,Cy,Hy,Ak,N

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 26:CLASS 29:CLASS 30:CLASS

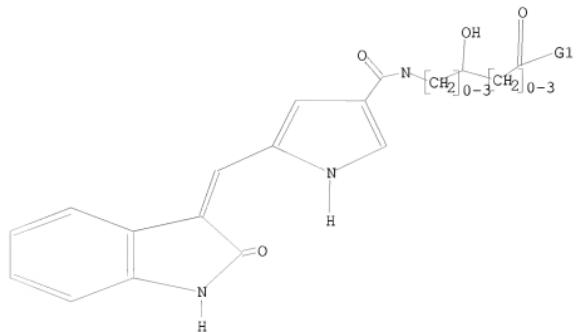
32:CLASS 34:CLASS

10580670.trn 10/13/2009

Page 11

L13 STRUCTURE UPLOADED

=&gt; d 113

L13 HAS NO ANSWERS  
L13 STR

G1 CH,NH2,Cy,Hy,Ak,N

Structure attributes must be viewed using STN Express query preparation.

=&gt; s 113

SAMPLE SEARCH INITIATED 11:36:19 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 58 TO ITERATE100.0% PROCESSED 58 ITERATIONS  
SEARCH TIME: 00.00.01

34 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 704 TO 1616  
PROJECTED ANSWERS: 331 TO 1029

L14 34 SEA SSS SAM L13

=> s 113 sss full  
FULL SEARCH INITIATED 11:36:31 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 1068 TO ITERATE100.0% PROCESSED 1068 ITERATIONS  
SEARCH TIME: 00.00.01

513 ANSWERS

L15 513 SEA SSS FUL L13

=> FIL HCPLUS	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	935.64	935.86

FILE 'HCPLUS' ENTERED AT 11:36:37 ON 13 JUL 2009  
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FILE COVERS 1907 - 13 Jul 2009 VOL 151 ISS 3  
 FILE LAST UPDATED: 12 Jul 2009 (20090712/ED)  
 REVISED CLASS FIELDS (NCL) LAST RELOADED: Apr 2009  
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

HCPlus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

CAS Information Use Policies apply and are available at:

<http://www.cas.org/legal/infopolicy.html>

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 11:25:28 ON 13 JUL 2009)

FILE 'REGISTRY' ENTERED AT 11:25:50 ON 13 JUL 2009

L1	STRUCTURE UPLOADED
L2	0 S L1
L3	0 S L1 SSS FULL
L4	STRUCTURE UPLOADED
L5	0 S L4
L6	0 S L4 SSS FULL
L7	STRUCTURE UPLOADED
L8	46 S L7
L9	853 S L8 SSS FULL
L10	STRUCTURE UPLOADED
L11	34 S L10
L12	520 S L10 SSS FULL
L13	STRUCTURE UPLOADED
L14	34 S L13

L15 513 S L13 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:36:37 ON 13 JUL 2009

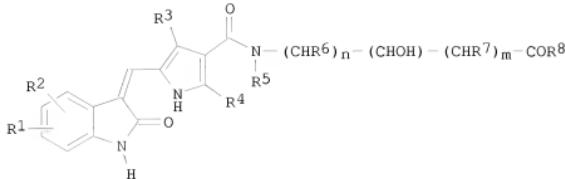
=> s 115  
L16 4 L15=> s 116 and py<=2003  
24035901 PY<=2003  
L17 0 L16 AND PY<=2003

=&gt; d 116 ibib abs tot

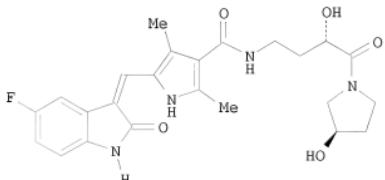
L16 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2006:1342422 HCAPLUS  
 DOCUMENT NUMBER: 146:81764  
 TITLE: Enhanced indolinone based protein kinase inhibitors  
 and their preparation, pharmaceutical compositions and  
 use in the treatment of cancer  
 INVENTOR(S): Liang, Congxin; Feng, Yangbo; Vojkovsky, Tomas  
 PATENT ASSIGNEE(S): The Scripps Research Institute, USA  
 SOURCE: U.S. Pat. Appl. Publ., 78pp., Cont.-in-part of Appl.  
 No. PCT/US2004/39725.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060287381	A1	20061221	US 2006-441537	20060526
WO 2005053686	A1	20050616	WO 2004-US39752	20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			WO 2004-US39752	A2 20041126
			US 2005-685144P	P 20050526
			US 2005-754360P	P 20051228
			US 2003-525430P	P 20031126
			US 2004-545721P	P 20040218

OTHER SOURCE(S): MARPAT 146:81764  
 GI



I



II

**AB** Hydroxy carboxy pyrrolyl-indolinone derivs. of formula I have enhanced and unexpected drug properties as inhibitors of protein kinases and are useful in treating disorders related to abnormal protein kinase activities such as cancer. More particularly, alpha-hydroxy-omega-(2-oxo-indolylidenemethyl-pyrrole-3'-carbonyl) amino alcanoic acid and amide derivs. have enhanced and unexpected drug properties as inhibitors of protein kinases with respect to their corresponding beta-hydroxy-omega-(2-oxo-indolylidenemethyl-pyrrole-3'-carbonyl) amino alcanoic acid and amide derivs. and are useful in treating disorders related to abnormal protein kinase activities such as cancer. Compound of formula I wherein R1 and R2 are independently H, halo, C1-6 (halo)alkyl, C3-8 cycloalkyl, OH, amino, etc.; R3 is H, C1-6 alkyl, C6-10 aryl, C5-10 heteroaryl, and amide; R3 - R6 are independently H and C1-6 alkyl; R7 is H, C1-6 alkyl, and OH; R8 is OH, C1-6 O-alkyl, C3-8 cycloalkyl and NH2 and derivs., etc.; n and m are independently 0, 1, 2, and 3; and their pharmaceutically acceptable salts, tautomers, and prodrugs thereof, are claimed. Example compound II was prepared by amidation of (S)-4-((15-[5-fluoro-2-oxo-1,2-dihydroindol-1(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carbonyl)amino)-2-hydroxybutyric acid with (R)-3-hydroxypyrrolidine. All the invention compds. were evaluated for their protein kinase inhibitory activity. From the assay, it was determined that compound II exhibited and IC50 value of < 0.003  $\mu$ M.

L16 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1252701 HCPLUS

DOCUMENT NUMBER: 146:27724

TITLE: Preparation of (pyrrolylmethylidene)indolinones as protein kinase inhibitors for the treatment of cancer

INVENTOR(S): Liang, Congxin; Feng, Yangbo; Vojkovsky, Tomas

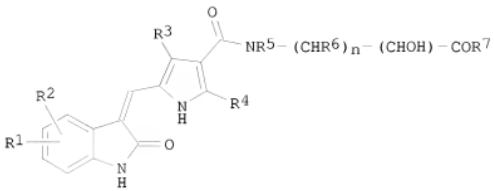
PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 49pp.

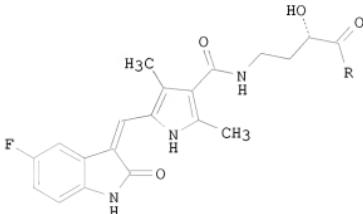
CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006127961	A1	20061130	WO 2006-US20363	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2006249790	A1	20061130	AU 2006-249790	20060526
CA 2610067	A1	20061130	CA 2006-2610067	20060526
EP 1893194	A1	20080305	EP 2006-771248	20060526
R: AI, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008542294	T	20081127	JP 2008-513740	20060526
MX 2007014810	A	20080221	MX 2007-14810	20071126
IN 2007DΝ09747	A	20080620	IN 2007-DΝ9747	20071217
KR 2008017058	A	20080225	KR 2007-730412	20071226
CN 101222920	A	20080716	CN 2006-80025908	20080115
PRIORITY APPLN. INFO.:			US 2005-685144P	P 20050526
			US 2005-754360P	P 20051228
			WO 2006-US20363	W 20060526

OTHER SOURCE(S): CASREACT 146:27724; MARPAT 146:27724  
 GI



I



II

**AB**  $\alpha$ -Hydroxy- $\omega$ -[5-(2-oxo-indol-3-ylidenemethyl)pyrrol-3-ylcarbonylamino]alkanoic acids and their derivs. I [wherein R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl, (hetero)aryl or amide; R4 - R6 = H or alkyl; R7 = OH, O-(alkyl), O-(cyclo)alkyl or (un)substituted amino; n = 1-3] and pharmaceutically acceptable salts, tautomers and prodrugs thereof were prepared as protein kinase inhibitors. For instance, II (R = OH) was synthesized via successive treatment of the corresponding pyrrolecarboxylic acid with HATU, amidation of the resultant active ester with Me (2S)-4-amino-2-hydroxybutyrate hydrochloride, and ester hydrolysis. Further amidation of acid II (R = OH) with amines led to a number of amides, such as III (R = NMe<sub>2</sub>, III). III had an IC<sub>50</sub> of < 0.003  $\mu$ M against KDR in VEGFR biochemical assay. Therefore, the invented compds. are useful in treating disorders related to abnormal protein kinase activities such as cancer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:523281 HCPLUS

DOCUMENT NUMBER: 143:59818

TITLE: Preparation of 2-[(2-oxo-1,2-dihydro-indol-3-ylidene)methyl]pyrrole-4-carboxamide derivatives as protein kinase inhibitors

INVENTOR(S): Liang, Congxin

PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

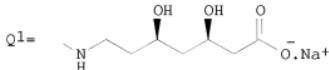
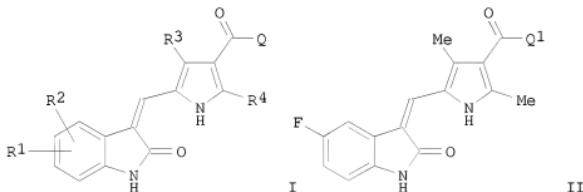
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053686	A1	20050616	WO 2004-US39752	20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, MZ, NA, NL, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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US 20060287381	A1	20061221	US 2006-441537	20060526
MX 2006006050	A	20070524	MX 2006-6050	20060526
PRIORITY APPLN. INFO.:				
			US 2003-525430P	P 20031126
			US 2004-545721P	P 20040218
			WO 2004-US39752	A2 20041126
			US 2005-685144P	P 20050526
			US 2005-754360P	P 20051228

OTHER SOURCE(S): CASREACT 143:59818; MARPAT 143:59818  
GI



AB The title compds. (I) [wherein R1 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, C1-6 alkoxy, NH2, C1-6 alkylamino, amide, sulfonamide, cyano, (un)substituted C6-10 aryl; R2 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, C1-6 alkoxy, C2-8 alkoxyalkyl, NH2, C1-6 alkylamino, C6-10 arylamino; R3 = H, C1-6 alkyl, C6-10 aryl, C5-10

heteroaryl, amide; R4-R6 = H, C1-6 alkyl; R7 = H, C1-6 alkyl, HO; R8 = HO, C1-6 alkoxy, C3-8 cycloalkoxy, NR9R10 (where R9, R10 = H, C1-6 alkyl, C1-6 hydroxyalkyl, C1-6 dihydroxyalkyl, C1-6 alkoxy, C1-6 alkylcarboxylic acid, C1-6 alkylphosphoric acid, C1-6 alkylsulfuric acid, C1-6 hydroxyalkylcarboxylic acid, C1-6 alkyl amide, C3-8 cycloalkyl, C5-8 heterocycloalkyl, C6-8 aryl, C5-8 heteroaryl, C3-8 cycloalkylcarboxylic acid; or NR9R10 together forms (un)substituted (C5-C8) heterocyclic); n, m = 0-3; p = 1-3] or pharmaceutically acceptable salts, their tautomers, pharmaceutically acceptable salts of their tautomer, or prodrugs thereof are prepared. These compds. have enhanced and unexpected drug properties as inhibitors of protein kinases, in particular VEGF receptors and PDGF receptors, and are useful in treating disorders related to abnormal protein kinase activities such as cancer (no data). Thus, 5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid was condensed with (4R,6R)-[6-(2-aminoethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetic acid tert-Bu ester using 3-dimethylaminopropyl-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole in DMF at room temperature for 30 h followed by treatment with a mixture of 2 N aqueous HCl, THF, and EtOH, neutralization with aqueous NaHCO<sub>3</sub>, extraction with Me tert-Bu ether to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxyl]amino]-3,5-dihydroxyheptanoic acid tert-Bu ester which was stirred with a mixture of aqueous NaOH solution and MeOH at room temperature for 3 h to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxyl]amino]-3,5-dihydroxyheptanoic acid sodium salt (II).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:523237 HCPLUS

DOCUMENT NUMBER: 143:59816

TITLE: Preparation of advanced indolinone based protein kinase inhibitors

INVENTOR(S): Liang, Congxin

PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

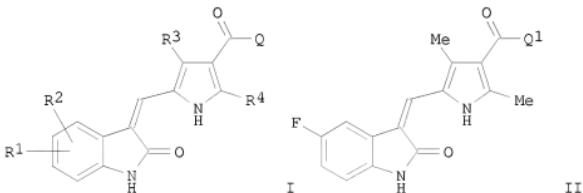
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

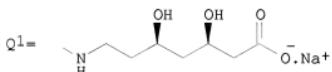
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WO 2005053614	A2	20050616	WO 2004-US39728	20041126
WO 2005053614	A3	20060223		
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SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004294981	A1	20050616	AU 2004-294981	20041126
CA 2547066	A1	20050616	CA 2004-2547066	20041126
EP 1686987	A2	20060809	EP 2004-812287	20041126
R: AT, BE, CH, IE, SI, LT, HR, IS, YU	DE, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK,			
CN 1905869	A	20070131	CN 2004-80040854	20041126
BR 200416994	A	20070206	BR 2004-16994	20041126
JP 2007512353	T	20070517	JP 2006-541462	20041126
MX 200606049	A	20070524	MX 2006-6049	20060526
IN 2006DN03108	A	20070824	IN 2006-DN3108	20060531
US 20080044881	A1	20080221	US 2007-580670	20070412
PRIORITY APPLN. INFO.:			US 2003-525430P	P 20031126
			US 2004-545721P	P 20040218
			WO 2004-US39728	W 20041126

OTHER SOURCE(S): CASREACT 143:59816; MARPAT 143:59816  
GI



$$Q = -NR^6-(CHR^6)_p-[CH(OH)-(CHR^7)_m]_p-COR^8$$



AB 2-[(2-Oxo-1,2-dihydro-indol-3-ylidene)methyl]pyrrole-4-carboxamide derivs. (I) wherein R1 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, C1-6 alkoxy, NH2, C1-6 alkylamino, amide, sulfonamide, cyano, (un)substituted C6-10 aryl; R2 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, C1-6 alkoxy, C2-8 alkoxyalkyl, NH2, C1-6 alkylamino, C6-10 arylamino; R3 = H, C1-6 alkyl, C6-10 aryl, C5-10 heteroaryl, amide; R4-R6 = H, C1-6 alkyl; R7 = H, C1-6 alkyl, HO; R8 = HO, C1-6 alkoxy, C3-8 cycloalkoxy, NR9R10 (where R9, R10 = H, C1-6 alkyl, C1-6 hydroxalkyl, C1-6 dihydroxyalkyl, C1-6 alkoxy, C1-6 alkylcarboxylic acid, C1-6 alkylphosphoric acid, C1-6 alkylsulfuric acid, C1-6 hydroxalkylcarboxylic acid, C1-6 alkyl amide, C3-8 cycloalkyl, C5-8 heterocycloalkyl, C6-8 aryl,

C5-8 heteroaryl, C3-8 cycloalkylcarboxylic acid; or NR9R10 together forms (un)substituted (C5-C8) heterocyclic; n, m = 0-3; p = 1-3] or pharmaceutically acceptable salts, their tautomers, pharmaceutically acceptable salts of their tautomer, or prodrugs thereof are prepared. These compds. have enhanced and unexpected drug properties as inhibitors of protein kinases, in particular VEGF receptors and PDGF receptors, and are useful in treating disorders related to abnormal protein kinase activities such as cancer (no data). Thus, 5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid was condensed with (4R,6R)-[6-(2-aminoethyl)-2,2-dimethyl-[1,3]dioxan-4-yl]acetic acid tert-Bu ester using 3-dimethylaminopropyl-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole in DMF at room temperature for 30 h followed by treatment with a mixture of 2 N aqueous HCl, THF, and EtOH, neutralization with aqueous NaHCO<sub>3</sub>, extraction with Me tert-Bu ether to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carbonyl]amino]-3,5-dihydroxyheptanoic acid tert-Bu ester which was stirred with a mixture of aqueous NaOH solution and MeOH at room temperature for 3 h to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carbonyl]amino]-3,5-dihydroxyheptanoic acid sodium salt (II).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 11:25:50 ON 13 JUL 2009

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L11	34 S L10
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L13	STRUCTURE UPLOADED
L14	34 S L13
L15	513 S L13 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:36:37 ON 13 JUL 2009

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L20 ANSWER 1 OF 8 HCPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2003:931518 HCPLUS  
 DOCUMENT NUMBER: 140:689  
 TITLE: Genes showing altered patterns of expression in  
 response to inhibition of tyrosine kinases and their  
 use in screening kinase inhibitors  
 INVENTOR(S): Morimoto, Alyssa; Deprimo, Samuel; O'Farrell,  
 Anne-Marie; Smolich, Beverly D.; Manning, William C.;  
 Walter, Sarah A.; Schilling, James Walter, Jr.;  
 Cherrington, Julie  
 PATENT ASSIGNEE(S): Sugen, Inc., USA  
 SOURCE: PCT Int. Appl., 408 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

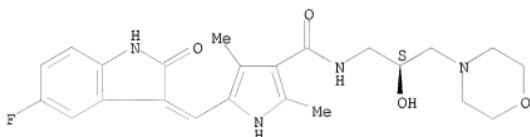
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003097854	A2	20031127	WO 2003-US15711	20030519 <--
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AU 2003233576	A1	20031202	AU 2003-233576	20030519 <--
US 20040018528	A1	20040129	US 2003-440464	20030519
PRIORITY APPLN. INFO.:			US 2002-380872P	P 20020517
			US 2003-448874P	P 20030224
			US 2003-448922P	P 20030224
			WO 2003-US15711	W 20030519

OTHER SOURCE(S): MARPAT 140:689

AB Genes that are regulated by tyrosine kinase-dependent signal transduction pathways are identified as markers for the screening of inhibitors of kinase activity. The change in levels of either the protein or mRNA in a suitable test system may be used to assess the effectiveness of a test compound as an inhibitor of a tyrosine kinase activity. The invention also relates to novel methods, wherein a change in the level of at least one biomarker in a mammal exposed to a compound, compared to the level of the biomarker(s) in a mammal that has not been exposed to the compound, indicates whether the mammal is being exposed to, or is experiencing or will experience a therapeutic or toxic effect in response to, a compound

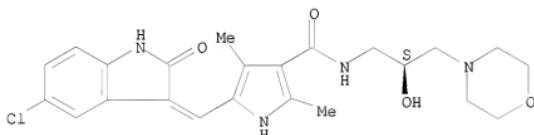
that inhibit tyrosine kinase activity.  
 IT 627908-92-3 627908-93-4 627908-94-5  
 627908-95-6  
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (as tyrosine kinase inhibitor; genes showing altered patterns of  
 expression in response to inhibition of tyrosine kinases and their use  
 in screening kinase inhibitors)  
 RN 627908-92-3 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-  
 ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl-  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



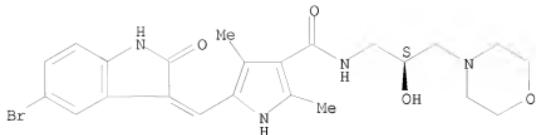
RN 627908-93-4 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-  
 ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl-  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



RN 627908-94-5 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-  
 ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl-  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

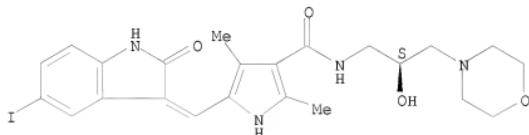


RN 627908-95-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-5-iodo-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



L20 ANSWER 2 OF 8 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:678808 HCPLUS

DOCUMENT NUMBER: 139:214331

TITLE: Process for preparing aminocarbonylpyrrolylmethylenindolinones from indolinones, imidazolcarbonylpyrrolecarboxaldehydes, and amines.

INVENTOR(S): Jin, Qingwu; Mauragis, Michael A.; May, Paul D.

PATENT ASSIGNEE(S): Pharmacia &amp; Upjohn Company, USA

SOURCE: PCT Int. Appl., 51 pp.

CODEN: PIXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070725	A2	20030828	WO 2003-US4520	20030214 <--
WO 2003070725	A3	20040115		
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WO 2002066463 A1 20020829 WO 2002-US4407 20020215 <--

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CA 2475455 A1 20030828 CA 2003-2475455 20030214 <--

AU 2003216282 A1 20030909 AU 2003-216282 20030214 <--

EP 1476443 A2 20041117 EP 2003-742760 20030214

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BR 2003007721 A 20050125 BR 2003-7721 20030214

CN 1671693 A 20050921 CN 2003-803988 20030214

CN 1308326 C 20070404

JP 2005528344 T 20050922 JP 2003-569632 20030214

RU 2299209 C2 20070520 RU 2004-124711 20030214

TW 289560 B 20071111 TW 2003-92125614 20030917

IN 2004DN02019 A 20070810 IN 2004-DN2019 20040714

MX 2004006992 A 20041110 MX 2004-6992 20040719

HK 1078075 A1 20070713 HK 2005-109991 20051109

PRIORITY APPLN. INFO.: WO 2002-US4407 A 20020215

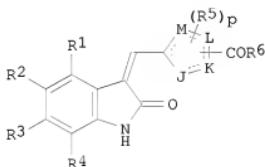
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US 2001-268683P P 20010215

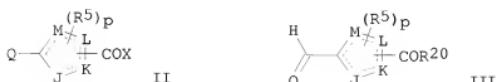
US 2001-312361P P 20010815

WO 2003-US4520 W 20030214

OTHER SOURCE(S): CASREACT 139:214331; MARPAT 139:214331  
GI



I



AB Title compds. [I; R1-R5 = H, alkyl, alkoxy, cycloalkyl, aryl, heterocyclyl

containing 1-3 N, S, O, aryloxy, alkaryl, alkaryloxy, halo, trihalomethyl, OH, SOR', SO2NR'R'', SO3R', SR', NO2, NR'R'', CN, COR', O2CR', NHCOR', (CH2)nCO2R', CONR'R''; R6 = NR8(CH2)nR9, NR10R11, 1-2 of the CH2 groups may be substituted by OH, halo; R8 = H, alkyl; R9 = NR10R11, OH, COR12, aryl, heterocyclyl containing 1-3 N, S, O, N+(O-)R10, NHCOR13; R10, R11 = H, alkyl, cyanoalkyl, cycloalkyl, aryl, heterocyclyl containing 1-3 N, S, O; R10R11N = (R'-substituted) 5-6 membered heterocyclyl optionally containing 1-3 addnl. N, O; R12 = H, OH, alkoxy, aryloxy; R13 = alkyl, haloalkyl, aralkyl; R', R'' = H, alkyl, cyanoalkyl, cycloalkyl, aryl, heterocyclyl containing 1-3 N, S, O; R'R''N = 5-6 membered heterocyclyl optionally containing 1-3 addnl. N, O; halo = F, Cl, Br, iod; J = O, S, NH; 1 of K, L, M = CCOR6, the others of K, L, M = CR5, CR52, N, NR5, O, S; n, p = 0-2; m = 1-4), were prepared. The process comprises reaction of azoles (II) with X2R (R5, J, K, L, M, p are as defined above; Q = CHO, CHS, dioxolanyl, tetrahydroooxazolyl, etc.; X1 = Cl, Br; X2 = H; R = pyrrolyl, thiazolidinethionyl, oxazolidinethionyl, imidazolidinethionyl, pyrrolidinethionyl, etc.; or X1 = OH, alkoxy, PhO; X2 = imidazolecarbonyl; R = imidazolyl) to give (III; R20 = OR, R), and reaction of III with HR6 (R6 as defined above) and the corresponding indolinone. Thus, 4-(1H-imidazol-1-ylcarbonyl)-3,5-dimethyl-1H-pyrrole-2-carboxaldehyde, N,N-diethylethylenediamine, 5-fluorooxindole, Et3N, and MeCN were mixed and heated for 18 h at 60° to give 85% N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide.

IT 452105-23-6P 452105-24-7P 452105-25-8P  
452105-26-9P

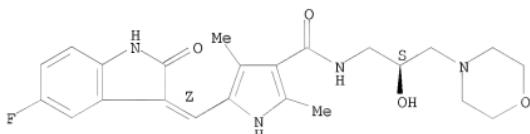
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process for preparing aminocarbonylpyrrolylmethylideneindolinones from indolinones, imidazolcarbonylpyrrolecarboxaldehydes, and amines)

RN 452105-23-6 HCPLUS

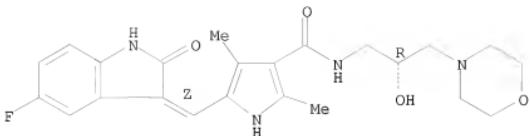
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



RN 452105-24-7 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

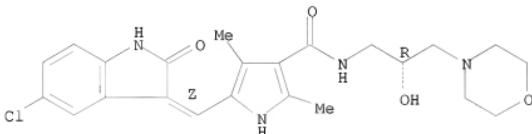


RN 452105-25-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

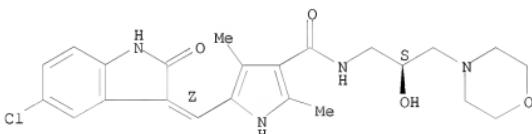


RN 452105-26-9 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 8 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:334853 HCPLUS

DOCUMENT NUMBER: 138:331677

TITLE: Treatment of acute myeloid leukemia with indolinone  
compounds, and preparation thereof

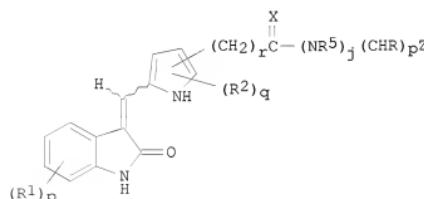
INVENTOR(S): O'Farrell, Ann-Marie; Cherrington, Julie

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: PCT Int. Appl., 76 pp.  
DOCUMENT TYPE: CODEN: PIXXD2  
LANGUAGE: Patent  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003035009	A2	20030501	WO 2002-US34525	20021028 <--
WO 2003035009	A3	20040318		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2464790	A1	20030501	CA 2002-2464790	20021028 <--
AU 2002360314	A1	20030506	AU 2002-360314	20021028 <--
AU 2002360314	B2	20070920		
US 20030130280	A1	20030710	US 2002-281266	20021028 <--
EP 1446117	A2	20040818	EP 2002-795563	20021028
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013960	A	20040831	BR 2002-13960	20021028
JP 2005511540	T	20050428	JP 2003-537578	20021028
HU 2005000422	A2	20051128	HU 2005-422	20021028
NZ 532405	A	20051223	NZ 2002-532405	20021028
CN 101052394	A	20071010	CN 2002-822959	20021028
ZA 2004003091	A	20050114	ZA 2004-3091	20040422
MX 2004003853	A	20050217	MX 2004-3853	20040423
PRIORITY APPLN. INFO.:			US 2001-330623P	P 20011026
			WO 2002-US34525	W 20021028

OTHER SOURCE(S): MARPAT 138:331677  
GI



1

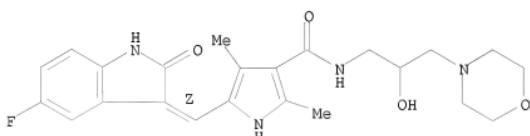
AB A method of treating acute myeloid leukemia in patient pos. for FLT-3-ITD

is described. The treatment is accomplished by administration of an indolinone compound (Markush included). Preparation of the compds. of the invention, e.g. I, is described.

IT 452104-85-7P 452104-87-9P 452105-23-6P  
452105-24-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(indolinone derivative preparation for treatment of acute myeloid leukemia)  
RN 452104-85-7 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

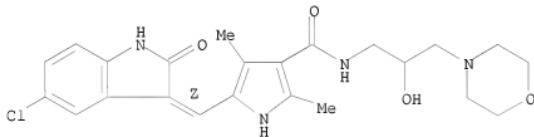
Double bond geometry as shown.



RN 452104-87-9 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.

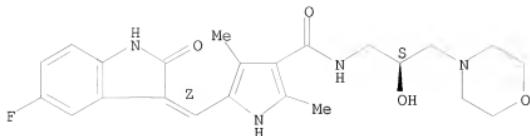


RN 452105-23-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

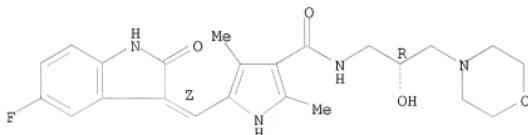


RN 452105-24-7 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



IT 452104-42-6P 452104-86-8P 452104-88-0P

452104-89-1P 452104-90-4P 452104-91-5P

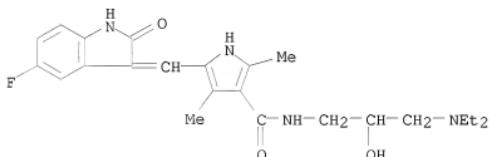
452104-92-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(indolinone derivative preparation for treatment of acute myeloid leukemia)

RN 452104-42-6 HCPLUS

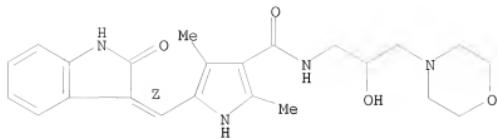
CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-86-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

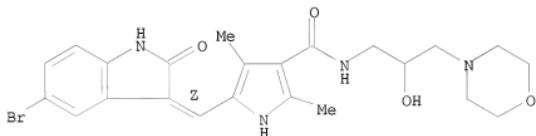
Double bond geometry as shown.



RN 452104-88-0 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

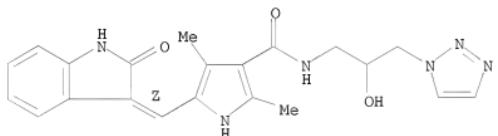
Double bond geometry as shown.



RN 452104-89-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

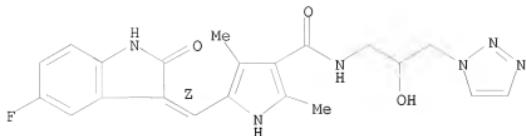
Double bond geometry as shown.



RN 452104-90-4 HCPLUS

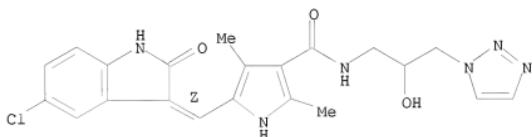
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



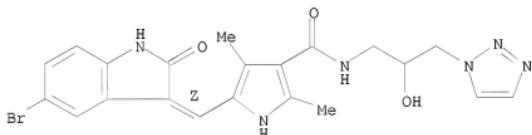
RN 452104-91-5 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl-  
 (CA INDEX NAME)

Double bond geometry as shown.



RN 452104-92-6 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl-  
 (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2003:154170 HCAPLUS  
 DOCUMENT NUMBER: 138:180703  
 TITLE: Combination therapy for the treatment of cancer  
 INVENTOR(S): Doshi, Parul; Cherrington, Julie  
 PATENT ASSIGNEE(S): Masferrer, Jaime, USA; Sugen Inc.  
 SOURCE: PCT Int. Appl., 217 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent

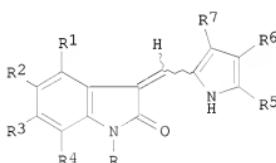
LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003015608	A2	20030227	WO 2002-US25797	20020815 <--
WO 2003015608	A3	20031030		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2457745	A1	20030227	CA 2002-2457745	20020815 <--
AU 2002329744	A1	20030303	AU 2002-329744	20020815 <--
AU 2002329744	B2	20070830		
US 20030216410	A1	20031120	US 2002-218910	20020815 <--
US 7320996	B2	20080122		
BR 2002011978	A	20040720	BR 2002-11978	20020815
CN 1541098	A	20041027	CN 2002-815912	20020815
JP 2005501843	T	20050120	JP 2003-520373	20020815
TW 230692	B	20050411	TW 2002-91118425	20020815
NZ 530792	A	20050930	NZ 2002-530792	20020815
HU 20050000424	A2	20070228	HU 2005-424	20020815
HU 20050000424	A3	20080428		
EP 1427326	B1	20081119	EP 2002-765988	20020815
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, SK, TR, AL, LT, LV, MK, RO, SI				
AT 414512	T	20081215	AT 2002-765988	20020815
IN 2004DN00220	A	20060224	IN 2004-DN220	20040129
ZA 2004000849	A	20050503	ZA 2004-849	20040202
NO 2004000516	A	20040413	NO 2004-516	20040204
MX 2004001464	A	20050217	MX 2004-1464	20040216
BG 108622	A	20051031	BG 2004-108622	20040308
PRIORITY APPLN. INFO.:			US 2001-312413P	P 20010815
			WO 2002-US25797	W 20020815

OTHER SOURCE(S):

MARPAT 138:180703

GI



AB The present invention relates to methods for treatment or prevention of neoplasia disorders using protein tyrosine kinase inhibitors in combination with cyclooxygenase inhibitors, in particular cyclooxygenase-2 selective inhibitors. The protein kinase inhibitors are of the formula I where R = H, piperazin-1-ylmethyl, 4-methylpiperazin-1-ylmethyl, piperidin-1-ylmethyl, etc.; R1 = H, halo, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, etc.; R2 = hydrogen, halo, alkyl, substituted alkyl, trihalomethyl, hydroxy, alkoxy, etc.; R3 = H, halogen, alkyl, substituted alkyl, trihalomethyl, hydroxy, alkoxy, aryl, heteroaryl, etc.; R4 = H, halogen, alkyl, substituted alkyl, hydroxy, alkoxy, etc.; R5 = H, alkyl, substituted alkyl, etc.; R6 = hydrogen, alkyl, substituted alkyl, etc.; and R7 = H, alkyl, substituted alkyl, aryl, heteroaryl, etc.

IT 1064444-33-2

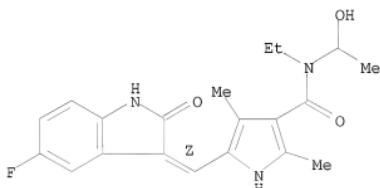
RL: PRPH (Prophetic)

(Combination therapy for the treatment of cancer)

RN 1064444-33-2 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, N-ethyl-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-(1-hydroxyethyl)-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:927188 HCAPLUS

DOCUMENT NUMBER: 138:14005

TITLE: Preparation of 5-aralkylsulfonyl-3-(pyrrol-2-ylmethylidene)-2-indolinone derivatives as kinase inhibitors

INVENTOR(S): Cui, Jingrong; Ramphal, Yudhi; Liang, Congxin; Sun, Li; Wei, Chung Chen; Tang, Peng Cho

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 479 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

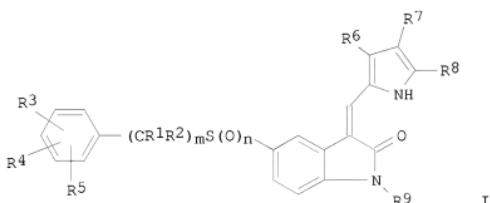
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2002096361	A2	20021205	WO 2002-US16841	20020530 <--

WO 2002096361	A3	20030313		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002303892	A1	20021209	AU 2002-303892	20020530 <--
US 20030125370	A1	20030703	US 2002-157007	20020530 <--
US 6599902	B2	20030729	WO 2002-US16841	
PRIORITY APPLN. INFO.:			US 2001-294544P	P 20010530
			US 2001-328408P	P 20011010
			WO 2002-US16841	W 20020530

OTHER SOURCE(S): MARPAT 138:14005  
GI



AB The present invention relates to certain 5-alkylsulfonyl-3-(pyrrol-2-ylmethylidene)-2-indolinone derivs. (shown as I; see below for variable definitions; e.g. 2,4-dimethyl-5-(2-oxo-5-phenylmethanesulfonyl-1,2-dihydroindol-(3Z)-ylidenemethyl)-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide) that inhibit kinases (no data), in particular met kinase. Pharmaceutical compns. comprising these compds., methods of treating diseases mediated by kinases using pharmaceutical compns. comprising these compds., and methods of preparing them are also disclosed. In I: n = 0-2; m = 1-3; R1 and R2 = H or alkyl; R3, R4, and R5 = H, halo, alkyl, cycloalkyl, haloalkyl, hydroxy, alkoxy, alkoxy carbonyl, haloalkoxy, cyano, carboxy, carboxyalkyl, nitro, aryl, aryloxy, heteroaryl, heteroaryloxy, -(alkylene)-CONR1OR11, -CONR10R11, or -NR10R11 (R10 is H or alkyl, and R11 is aryl, heteroaryl, heterocycle, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxyalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxycarbonylalkyl, heteroaralkyl, aralkyl, or heterocyclylalkyl wherein the alkyl chain in aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, aralkyl, heteroaralkyl, or heterocyclylalkyl is optionally substituted with one or two hydroxy, or R10 and R11 together with the N atom to which they are attached combine to form saturated or unsatd. heterocycloamino). R6 is H, alkyl, cycloalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,

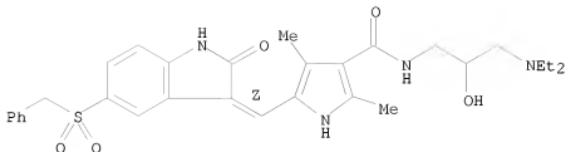
carboxyalkyl, heterocyclalkyl, aryl, heteroaryl, carboxy, alkoxy carbonyl, heterocyclic carbonyl, aminoalkyl carbonyl, alkylaminoalkyl carbonyl, dialkylaminoalkyl carbonyl,  $-\text{CONR10R11}$  or  $-(\text{alkylene})-\text{CONR10R11}$ . R<sub>7</sub> and R<sub>8</sub> = H, alkyl, cycloalkyl, heterocyclalkyl,  $-\text{COR12}$ ,  $-(\text{alkylene})-\text{COR12}$  (R<sub>12</sub> = alkoxy, hydroxy, or heterocyclic, alkylamino, dialkylamino),  $-\text{SO2R14}$ ,  $-\text{CONR13R14}$ , or  $-(\text{alkylene})-\text{CONR13R14}$  (R<sub>13</sub> is H or alkyl, and R<sub>14</sub> is aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, hydroxylalkyl, acetylalkyl, cyanoalkyl, carboxyalkyl, alkoxy carbonylalkyl, heteroaralkyl, or heterocyclalkyl wherein the alkyl chain in aminoalkyl, heteroaralkyl, heteroaralkyl, or heterocyclalkyl is optionally substituted with one or two hydroxy group(s), or when R<sub>13</sub> and R<sub>14</sub> are attached to a N atom R<sub>13</sub> and R<sub>14</sub> together with the N atom to which they are attached form saturated or unsatd. heterocycloamino). R<sub>6</sub> and R<sub>7</sub> or R<sub>7</sub> and R<sub>8</sub> can combine to form a saturated or unsatd. 5 to 8 membered ring; and R<sub>9</sub> is: H or alkyl;  $-\text{PO}(\text{OR15})_2$  where each R<sub>15</sub> = H or alkyl;  $-\text{COR16}$  where R<sub>16</sub> is H or alkyl; or  $-\text{CHR17NR18R19}$  where R<sub>17</sub> is H or alkyl, and R<sub>18</sub> and R<sub>19</sub> = H or alkyl or R<sub>18</sub> and R<sub>19</sub> together with the N atom to which they are attached form heterocycloamino. Although the methods of preparation are not claimed, 375 example preps. of I plus addnl. preps. of intermediates are included. [This abstract record is one of 2 records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.]

IT 477574-59-7P, 2,4-Dimethyl-5-(2-oxo-5-phenylmethanesulfonyl-1,2-dihydroindol-3-(Z)-ylidinemethyl)-1H-pyrrole-3-carboxylic acid  
 (3-diethylamino-2-hydroxypropyl)amide 477574-88-2P,  
 5-[5-(2,6-Dichlorophenylmethanesulfonyl)-2-oxo-1,2-dihydroindol-3-(Z)-ylidinemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid  
 (2-hydroxy-3-(morpholin-4-yl)propyl)amide 477574-89-3P,  
 5-[5-(2,6-Dichlorophenylmethanesulfonyl)-2-oxo-1,2-dihydroindol-3-(Z)-ylidinemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid  
 (2-hydroxy-3-[1,2,3]triazol-1-ylpropyl)amide 477576-51-5P,  
 5-[5-(2,6-Dichlorophenylmethanesulfonyl)-2-oxo-1,2-dihydroindol-3-(Z)-ylidinemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid  
 (2-hydroxy-3-(pyrrolidin-1-yl)propyl)amide 477576-52-6P,  
 5-[5-(2,6-Dichlorophenylmethanesulfonyl)-2-oxo-1,2-dihydroindol-3-(Z)-ylidinemethyl]-2,4-dimethyl-1H-pyrrole-3-carboxylic acid  
 (3-cyclopropylamino-2-hydroxypropyl)amide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug candidate; preparation of aralkylsulfonyl- and pyrrolylmethylenesubstituted indolinones as kinase inhibitors useful against cancers and other disorders)

RN 477574-59-7 HCPLUS

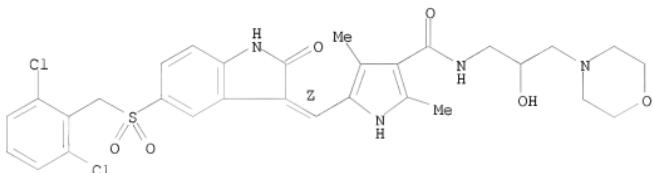
CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-[1,2-dihydro-2-oxo-5-[(phenylmethyl)sulfonyl]-3H-indol-3-ylidene]methyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



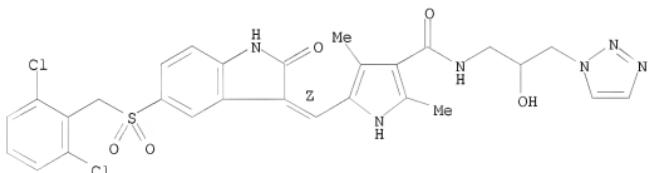
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Double bond geometry as shown.



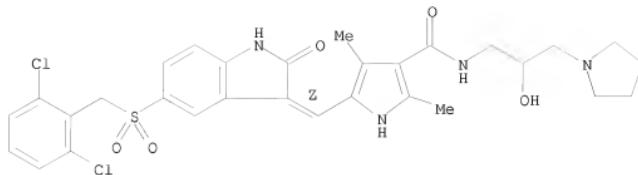
RN 477574-89-3 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[5-[(2,6-dichlorophenyl)methylsulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



RN 477576-51-5 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[5-[(2,6-dichlorophenyl)methylsulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(1-pyrrolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

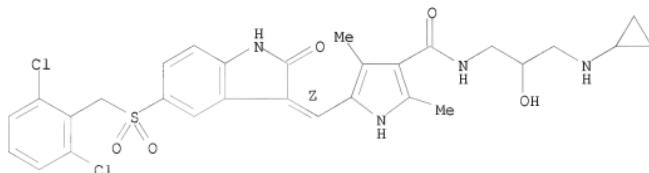
Double bond geometry as shown.



RN 477576-52-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(cyclopropylamino)-2-hydroxypropyl]-5-[(Z)-5-[(2,6-dichlorophenyl)methylsulfonyl]-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 8 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:1658111 HCPLUS

DOCUMENT NUMBER: 137:185408

TITLE: 3-(4-Amidopyrrol-2-ylmethylidene)-2-indolinone

derivatives as protein kinase inhibitors

INVENTOR(S): Guan, Huiping; Liang, Congxin; Sun, Li; Tang, Peng  
Cho, Wei; Chung Chen; Mauragis, Michael A.; Vojkovsky, Tomas; Jin, Qingwu; Herrinton, Paul Matthew

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 167 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

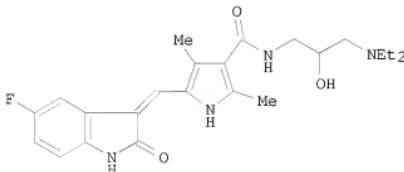
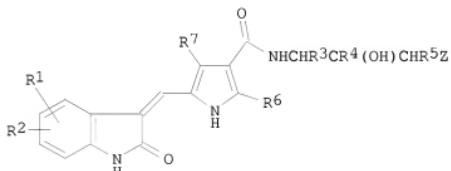
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NZ 527572 A 20050729	NZ 2002-527572	20020215	
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			US 2003-656907	A3 20030908
			US 2006-511981	A3 20060828

OTHER SOURCE(S) :  
GI

MARPAT 137:185408



AB Title compds. I [R1 = H, halo, alkyl, haloalkoxy, cycloalkyl, heterocyclic, OH, alkoxy, (un)esterified CO2H, (un)substituted NH2, CONH2; R2 = H, halo, alkyl, trihalomethyl, OH, alkoxy, CN, (un)substituted NH2, SO2NH2, (un)esterified CO2H, SO2R8; R8 = alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl; R3-R6 = H, alkyl; R7 = H, alkyl, aryl, heteroaryl, acyl; Z

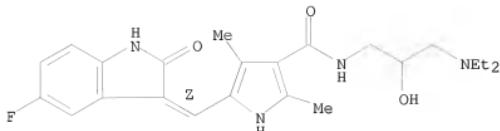
= aryl, heteroaryl, heterocyclic, (un)substituted NH<sub>2</sub>] were prepared for use as protein kinase inhibitors in treatment of diseases, such as cancer (no data). Thus, Et 3,5-dimethyl-4-pyrrolecarboxylate was oxidized to the 5-carboxaldehyde, followed by ester hydrolysis, reaction with 5-fluoro-2-oxindole and amidation to give the amide II.

IT 375798-55-3P 452104-42-6P 452104-43-7P  
 452104-44-8P 452104-45-9P 452104-46-0P  
 452104-47-1P 452104-48-2P 452104-49-3P  
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RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of 3-(4-amidopyrrol-2-ylmethyldene)-2-indolinone derivs. as protein kinase inhibitors)

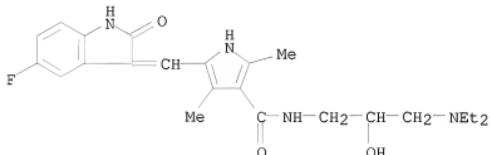
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 CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



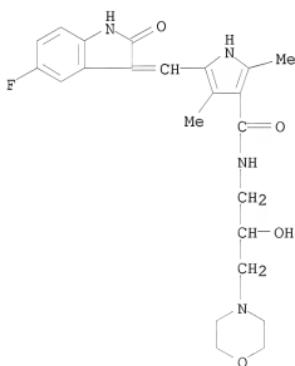
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RN 452104-43-7 HCAPLUS

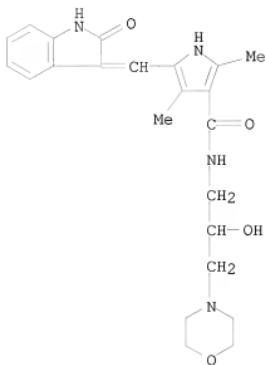
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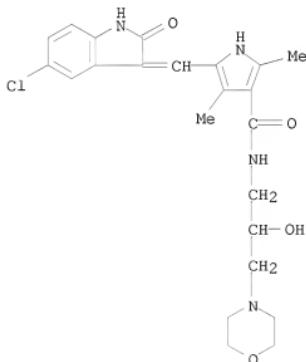
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CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)



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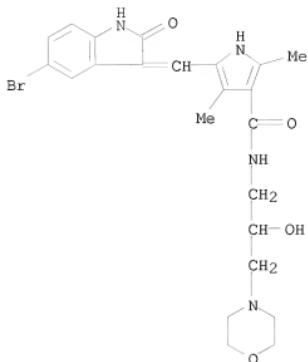
CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-46-0 HCAPLUS

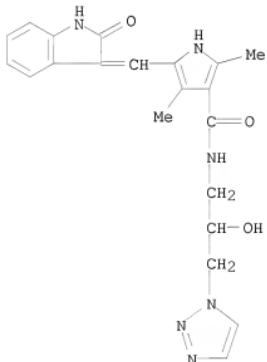
CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

INDEX NAME)



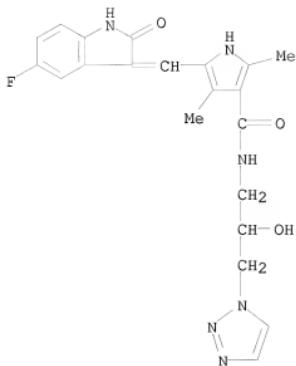
RN 452104-47-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)



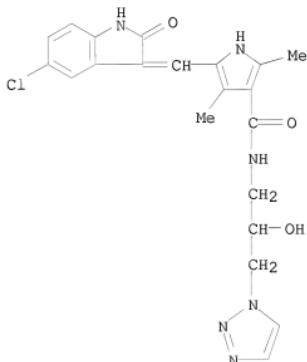
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CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)



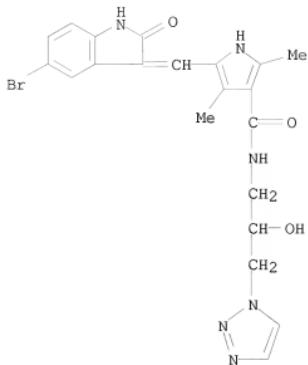
RN 452104-49-3 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

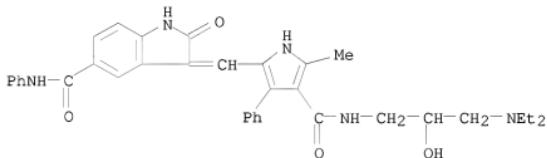


RN 452104-50-6 HCAPLUS

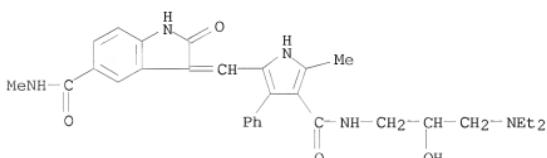
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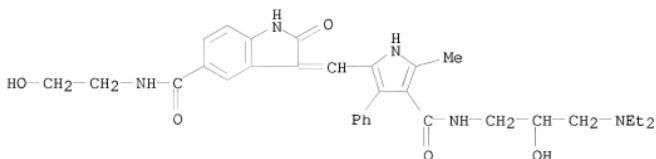
RN 452104-51-7 HCPLUS  
 CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxypropyl]amino)carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-phenyl- (CA INDEX NAME)



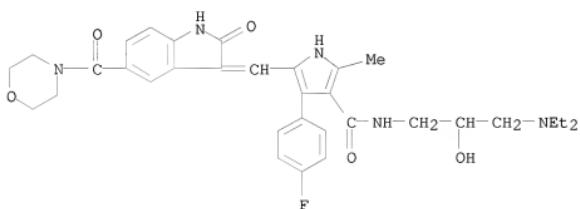
RN 452104-52-8 HCPLUS  
 CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxypropyl]amino)carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo- (CA INDEX NAME)



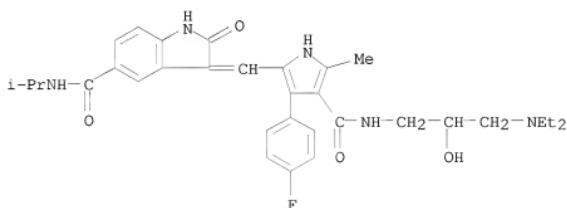
RN 452104-53-9 HCAPLUS  
 CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo- (CA INDEX NAME)



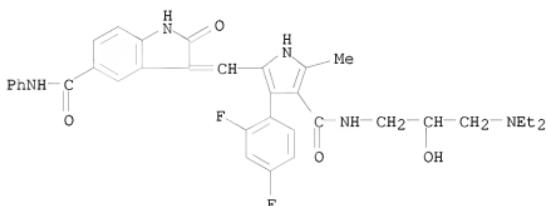
RN 452104-54-0 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[[1,2-dihydro-5-(4-morpholinylcarbonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(4-fluorophenyl)-2-methyl- (CA INDEX NAME)



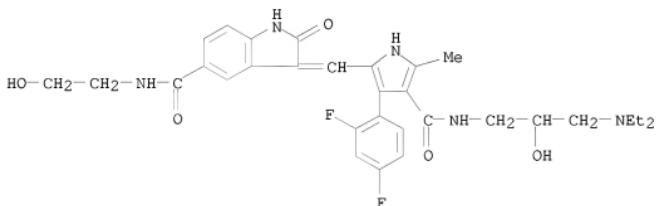
RN 452104-55-1 HCAPLUS  
 CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-3-(4-fluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (CA INDEX NAME)



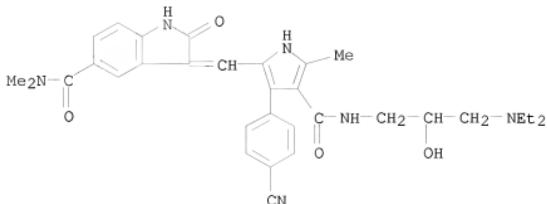
RN 452104-56-2 HCPLUS  
 CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-phenyl- (CA INDEX NAME)



RN 452104-57-3 HCPLUS  
 CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo- (CA INDEX NAME)

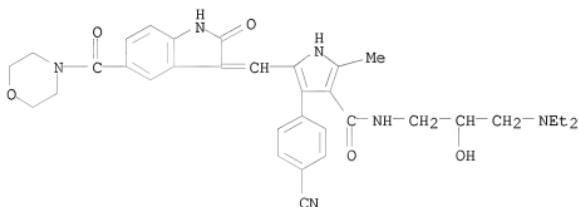


RN 452104-58-4 HCPLUS  
 CN 1H-Indole-5-carboxamide, 3-[[3-(4-cyanophenyl)-4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N,N-dimethyl-2-oxo- (CA INDEX NAME)



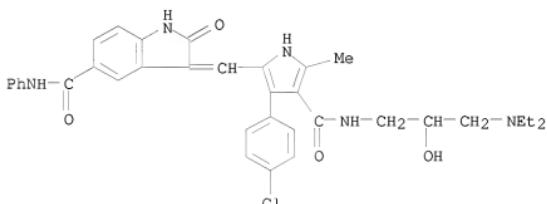
RN 452104-59-5 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 4-(4-cyanophenyl)-N-[3-(diethylamino)-2-hydroxypropyl]-5-[(1,2-dihydro-5-(4-morpholinylcarbonyl)-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl- (CA INDEX NAME)



RN 452104-60-8 HCPLUS

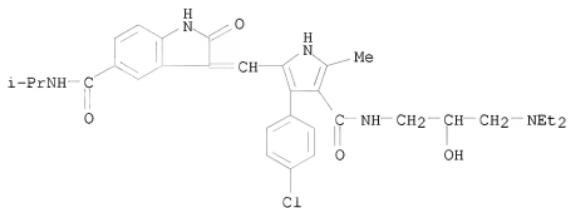
CN 1H-Indole-5-carboxamide, 3-[(3-(4-chlorophenyl)-4-[(3-(diethylamino)-2-hydroxypropyl)amino]carbonyl]-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-phenyl- (CA INDEX NAME)



RN 452104-61-9 HCPLUS

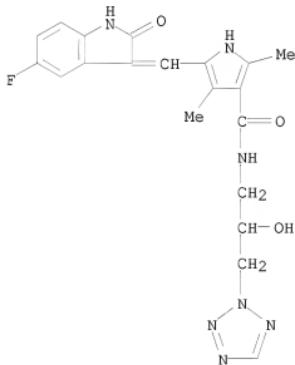
CN 1H-Indole-5-carboxamide, 3-[(3-(4-chlorophenyl)-4-[(3-(diethylamino)-2-

hydroxypropyl]amino]carbonyl]-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo- (CA INDEX NAME)



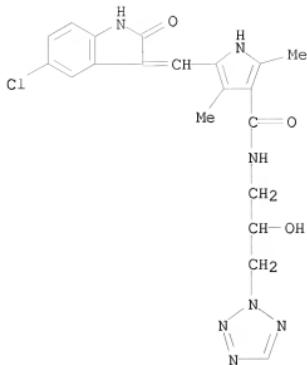
RN 452104-62-0 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

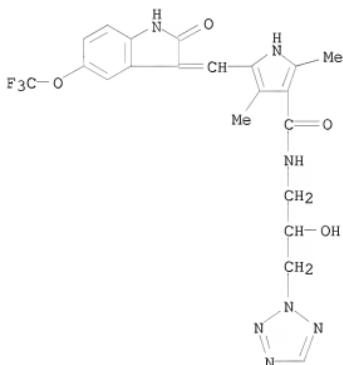


RN 452104-63-1 HCPLUS

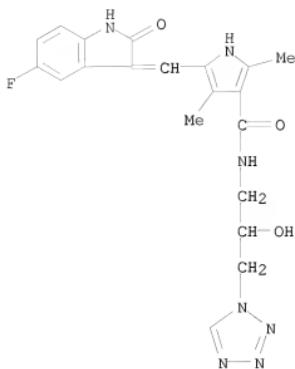
CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-64-2 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

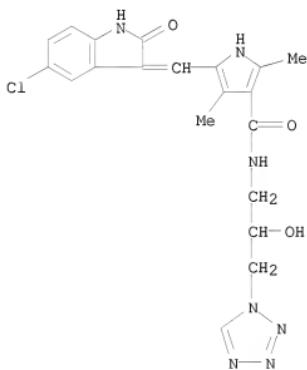


RN 452104-65-3 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)



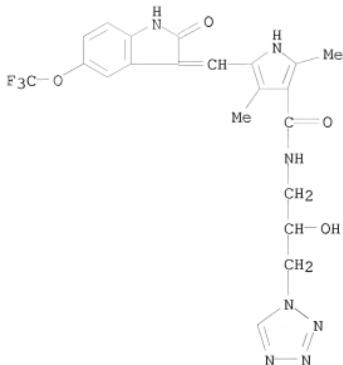
RN 452104-66-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)



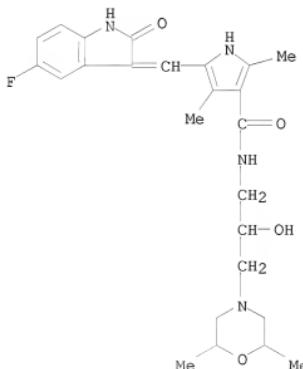
RN 452104-67-5 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)



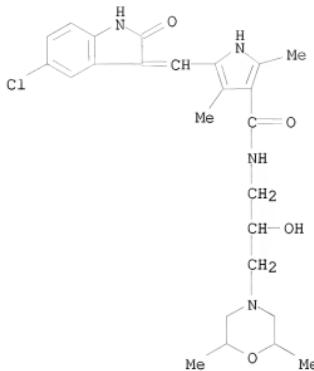
RN 452104-68-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(2,6-dimethyl-4-morpholinyl)-2-hydroxypropyl]-5-[5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)



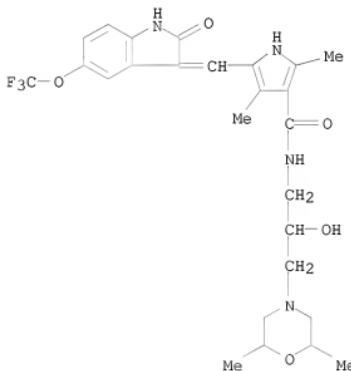
RN 452104-69-7 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(2,6-dimethyl-4-morpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)



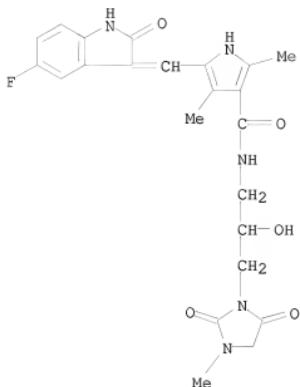
RN 452104-70-0 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[3-(2,6-dimethyl-4-morpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)



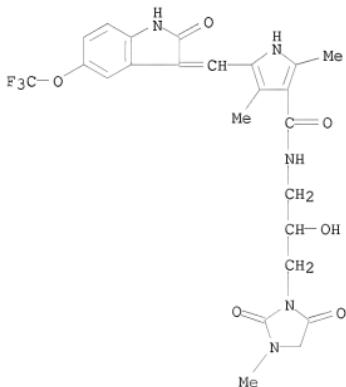
RN 452104-71-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-72-2 HCPLUS

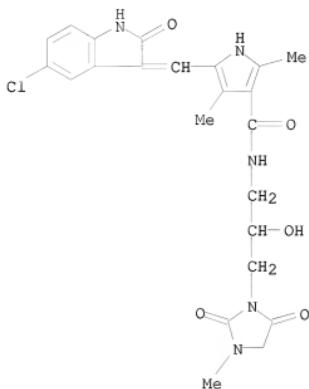
CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-73-3 HCPLUS

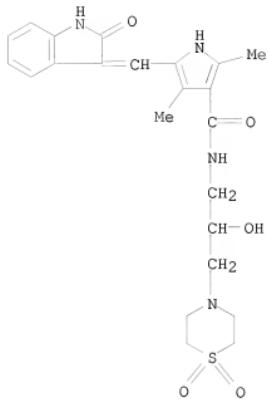
10580670

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)



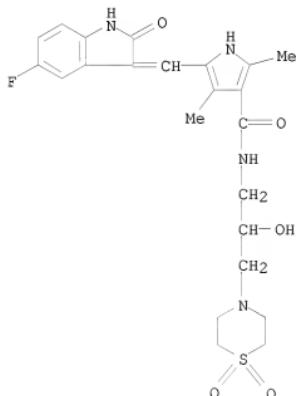
RN 452104-74-4 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-75-5 HCAPUS

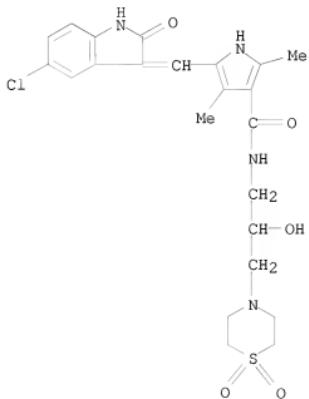
CN 1H-Pyrrole-3-carboxamide, N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-76-6 HCAPLUS

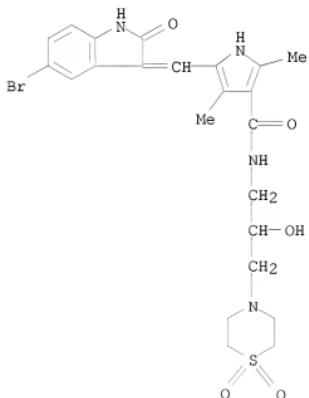
CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

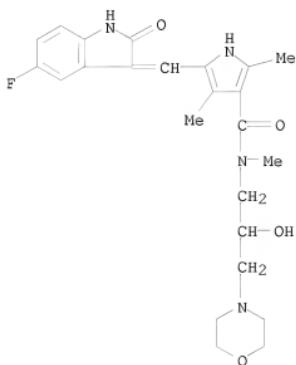


RN 452104-77-7 HCPLUS

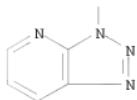
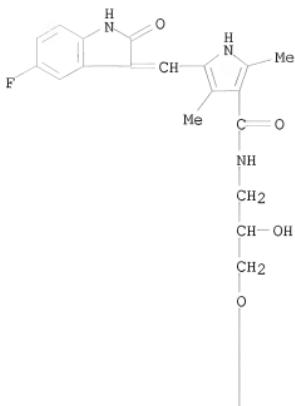
CN 1H-Pyrrole-3-carboxamide, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-78-8 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-N,2,4-trimethyl- (CA INDEX NAME)

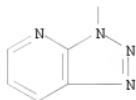
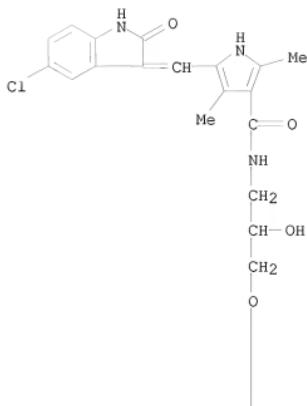


RN 452104-79-9 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yl oxy)propyl]-2,4-dimethyl- (CA INDEX NAME)



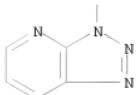
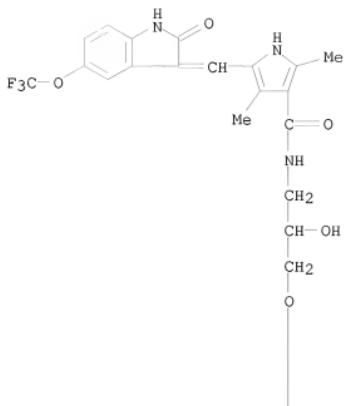
RN 452104-80-2 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yloxy)propyl]-2,4-dimethyl- (CA INDEX NAME)



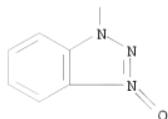
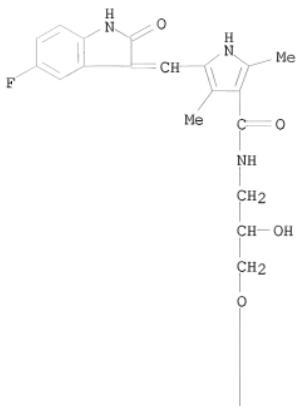
RN 452104-81-3 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yloxy)propyl]-2,4-dimethyl- (CA INDEX NAME)

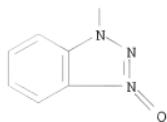
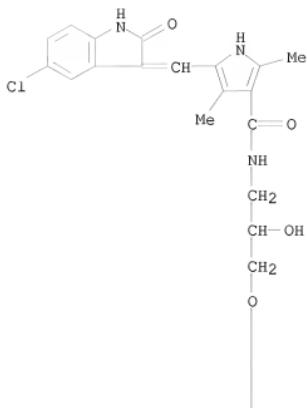


RN 452104-82-4 HCAPLUS

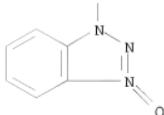
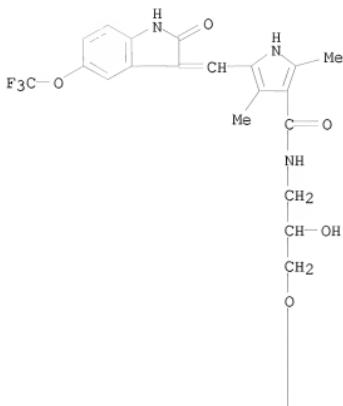
CN 1H-Pyrrole-3-carboxamide, 5-[(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-83-5 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)

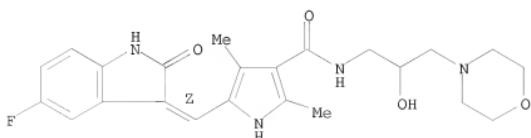


RN 452104-84-6 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)



RN 452104-85-7 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

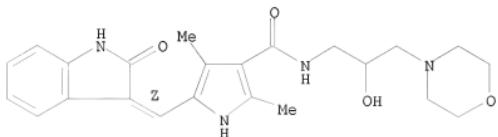
Double bond geometry as shown.



10580670

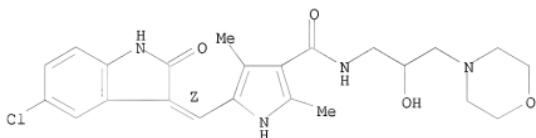
RN 452104-86-8 HCAPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



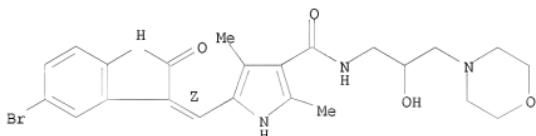
RN 452104-87-9 HCAPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



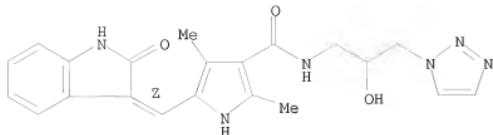
RN 452104-88-0 HCAPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



RN 452104-89-1 HCAPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

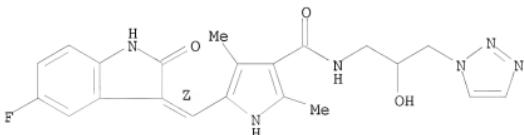
Double bond geometry as shown.



RN 452104-90-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

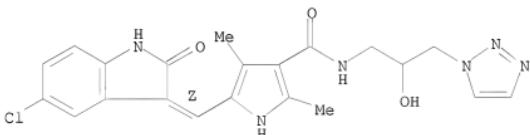
Double bond geometry as shown.



RN 452104-91-5 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

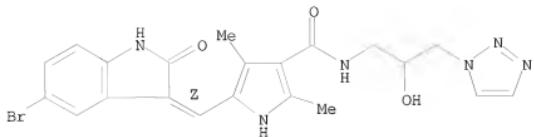
Double bond geometry as shown.



RN 452104-92-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

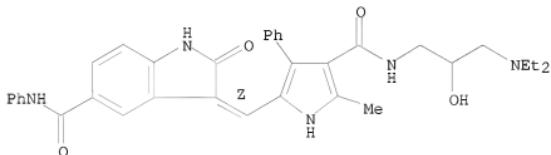
Double bond geometry as shown.



RN 452104-93-7 HCAPLUS

CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxypropyl]amino)carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-phenyl-, (3Z)- (CA INDEX NAME)

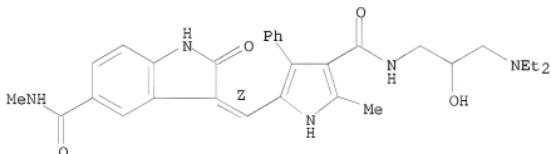
Double bond geometry as shown.



RN 452104-94-8 HCAPLUS

CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxypropyl]amino)carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-methyl-2-oxo-, (3Z)- (CA INDEX NAME)

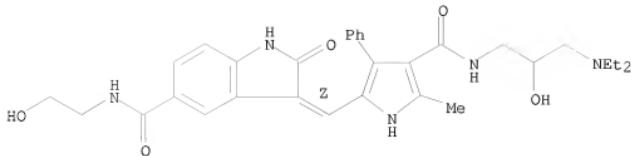
Double bond geometry as shown.



RN 452104-95-9 HCAPLUS

CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxyethyl]amino)carbonyl]-5-methyl-3-phenyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo-, (3Z)- (CA INDEX NAME)

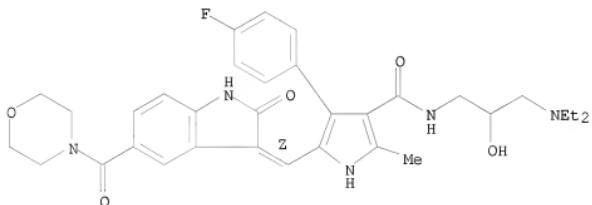
Double bond geometry as shown.



RN 452104-96-0 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[ (Z)-[1,2-dihydro-5-(4-morpholinylcarbonyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-(4-fluorophenyl)-2-methyl- (CA INDEX NAME)

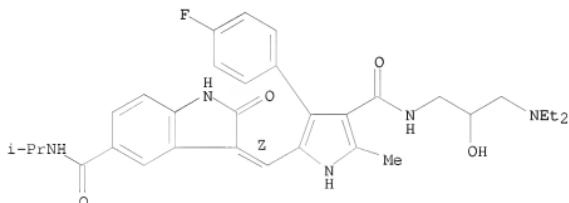
Double bond geometry as shown.



RN 452104-97-1 HCPLUS

CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-3-(4-fluorophenyl)-5-methyl-1H-pyrrol-2-yl]methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo-, (3Z)- (CA INDEX NAME)

Double bond geometry as shown.

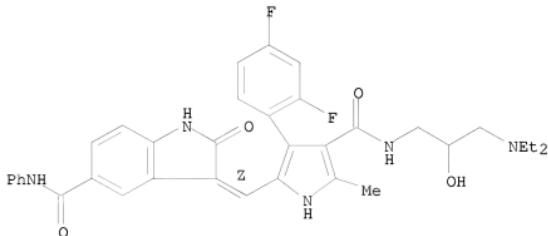


RN 452104-98-2 HCPLUS

CN 1H-Indole-5-carboxamide, 3-[[4-[[3-(diethylamino)-2-hydroxypropyl]amino]carbonyl]-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-

yl)methylene]-2,3-dihydro-2-oxo-N-phenyl-, (3Z)- (CA INDEX NAME)

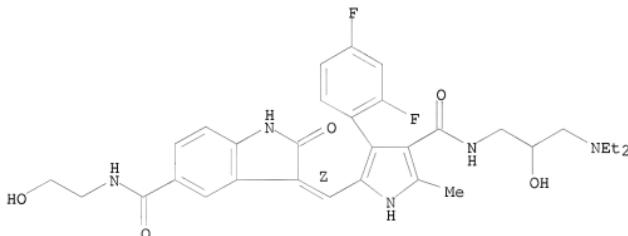
Double bond geometry as shown.



RN 452104-99-3 HCAPLUS

CN 1H-Indole-5-carboxamide, 3-[(4-[(3-(diethylamino)-2-hydroxypropyl]amino)carbonyl]-3-(2,4-difluorophenyl)-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-(2-hydroxyethyl)-2-oxo-, (3Z)- (CA INDEX NAME)

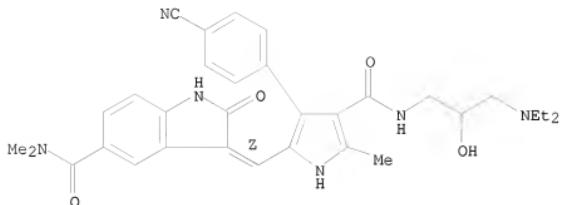
Double bond geometry as shown.



RN 452105-00-9 HCAPLUS

CN 1H-Indole-5-carboxamide, 3-[(3-(4-cyanophenyl)-4-[(3-(diethylamino)-2-hydroxypropyl)amino]carbonyl]-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N,N-dimethyl-2-oxo-, (3Z)- (CA INDEX NAME)

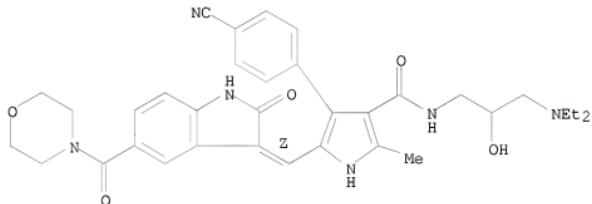
Double bond geometry as shown.



RN 452105-01-0 HCAPLUS

INN 4515-01-0  
CN 1H-Pyrrole-3-carboxamide, 4-(4-cyanophenyl)-N-[3-(diethylamino)-2-hydroxypropyl]-5-[1-(2,2-dihydro-5-(4-morpholinylcarbonyl)-2-oxo-3H-indol-3-ylidene)methyl]-2-methyl- (CA INDEX NAME)

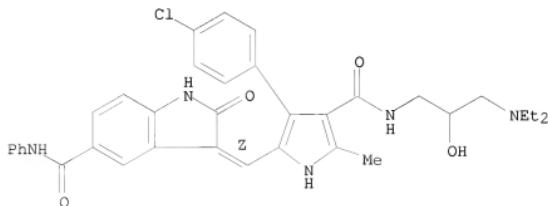
Double bond geometry as shown.



BN 452105-02-1 HCAPLUS

RN 45033-02-1 InchiKey: 5J1H-1M-5-carboxamide, 3-[(3-(4-chlorophenyl)-4-[(3-(diethylamino)-2-hydroxypropyl)amino]carbonyl]-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-2-oxo-N-phenyl-, (3Z)- (CA INDEX NAME)

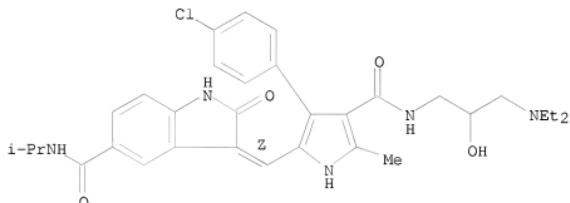
Double bond geometry as shown.



10580670

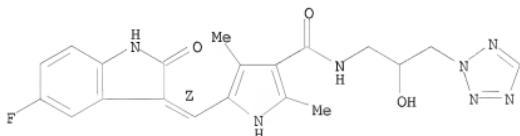
RN 452105-03-2 HCPLUS  
CN 1H-Indole-5-carboxamide, 3-[(3-(4-chlorophenyl)-4-[(3-(diethylamino)-2-hydroxypropyl)amino]carbonyl)-5-methyl-1H-pyrrol-2-yl)methylene]-2,3-dihydro-N-(1-methylethyl)-2-oxo-, (3Z)- (CA INDEX NAME)

Double bond geometry as shown.



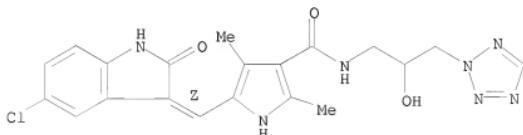
RN 452105-04-3 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



RN 452105-05-4 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

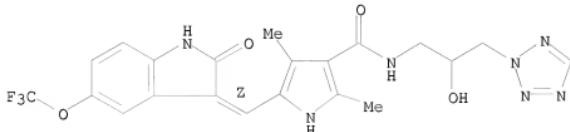
Double bond geometry as shown.



RN 452105-06-5 HCPLUS  
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-

3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-tetrazol-2-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

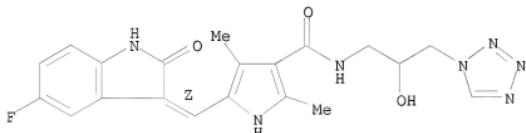
Double bond geometry as shown.



RN 452105-07-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

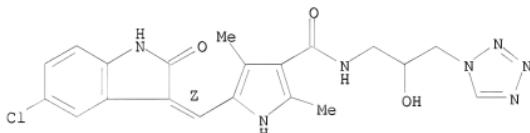
Double bond geometry as shown.



RN 452105-08-7 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

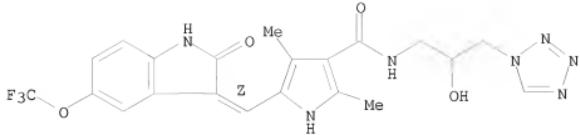
Double bond geometry as shown.



RN 452105-09-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1H-tetrazol-1-yl)propyl]-2,4-dimethyl-  
(CA INDEX NAME)

Double bond geometry as shown.

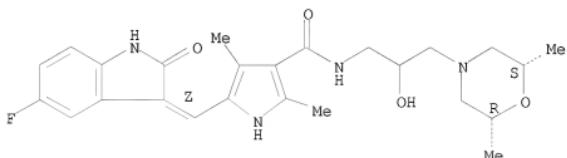


RN 452105-10-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-[(2R,6S)-2,6-dimethyl-4-morpholinyl]-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-, rel- (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

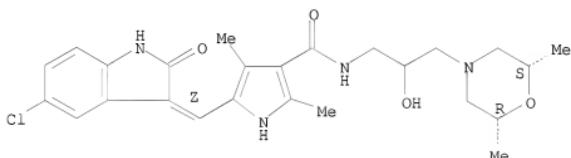


RN 452105-11-2 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-[(2R,6S)-2,6-dimethyl-4-morpholinyl]-2-hydroxypropyl]-2,4-dimethyl-, rel- (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

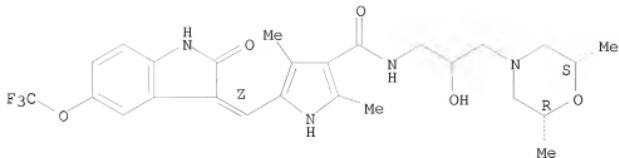


RN 452105-12-3 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[3-[(2R,6S)-2,6-dimethyl-4-morpholinyl]-2-hydroxypropyl]-2,4-dimethyl-, rel- (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry as shown.

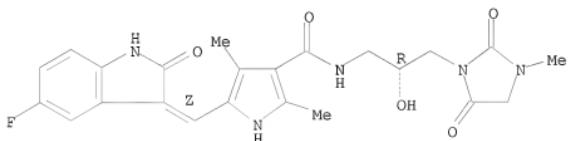


RN 452105-13-4 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

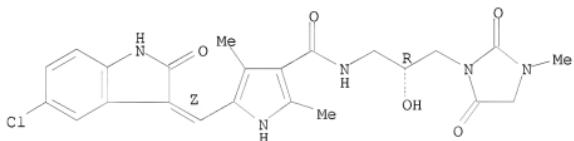


RN 452105-14-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

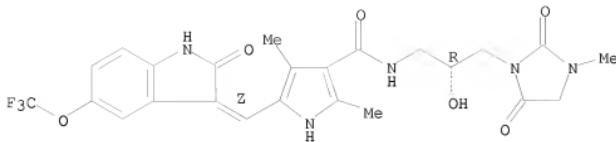


RN 452105-15-6 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene]methyl]-N-[(2R)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

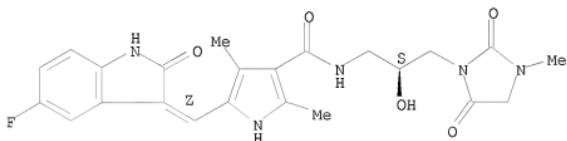


RN 452105-16-7 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

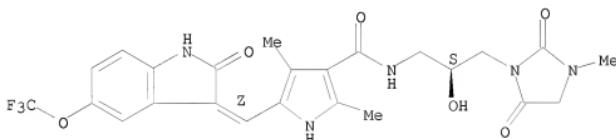


RN 452105-17-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

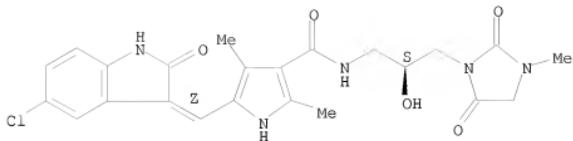


RN 452105-18-9 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(3-methyl-2,5-dioxo-1-imidazolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

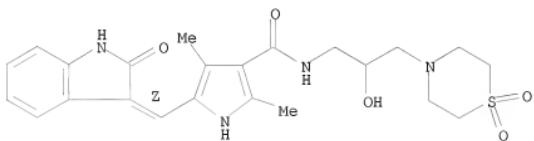
Absolute stereochemistry.

Double bond geometry as shown.



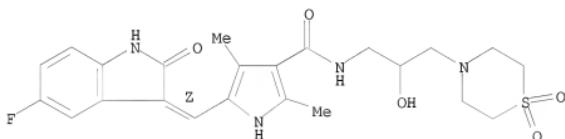
RN 452105-19-0 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



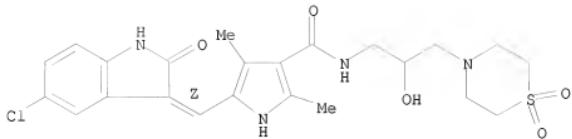
RN 452105-20-3 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



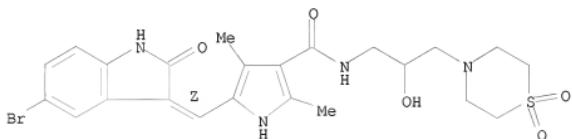
RN 452105-21-4 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



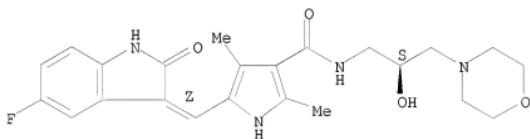
RN 452105-22-5 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



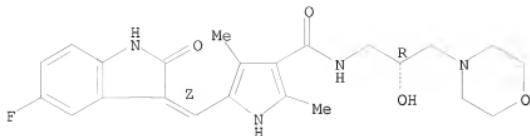
RN 452105-23-6 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.



RN 452105-24-7 HCAPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as shown.

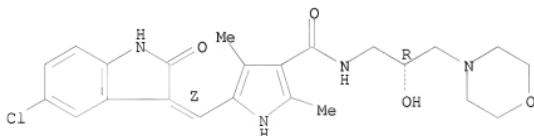


RN 452105-25-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

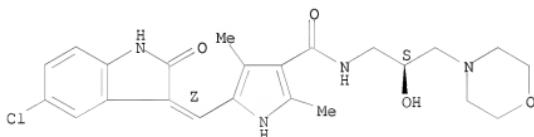


RN 452105-26-9 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

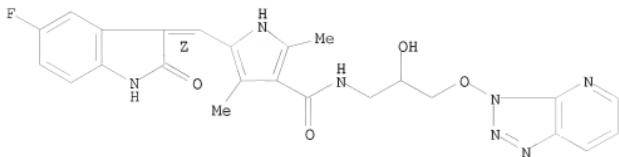
Double bond geometry as shown.



RN 452105-27-0 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

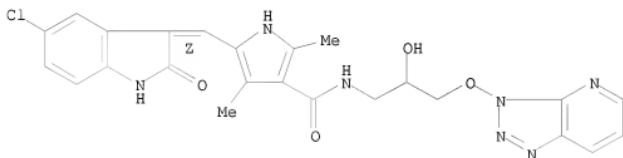
Double bond geometry as shown.



RN 452105-28-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yl)oxy]propyl- (CA INDEX NAME)

Double bond geometry as shown.

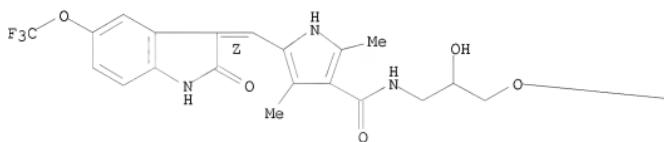


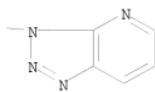
RN 452105-29-2 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(3H-1,2,3-triazolo[4,5-b]pyridin-3-yl)oxy]propyl- (CA INDEX NAME)

Double bond geometry as shown.

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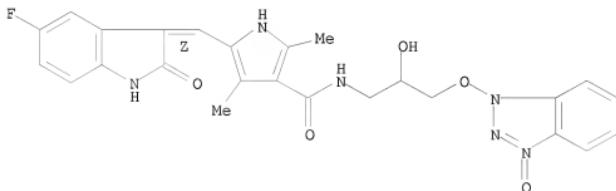




RN 452105-30-5 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)

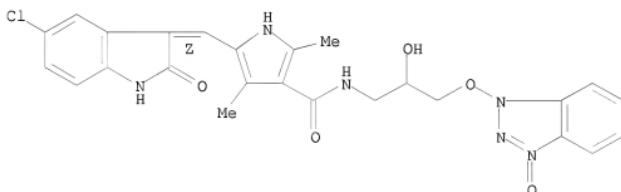
Double bond geometry as shown.



RN 452105-31-6 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.

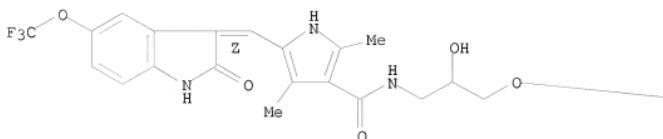


RN 452105-32-7 HCPLUS

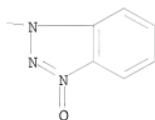
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[1,2-dihydro-2-oxo-5-(trifluoromethoxy)-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-[(3-oxido-1H-benzotriazol-1-yl)oxy]propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

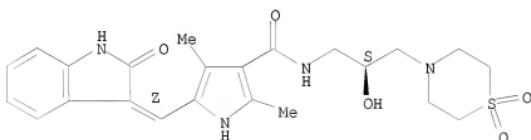


RN 452105-44-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

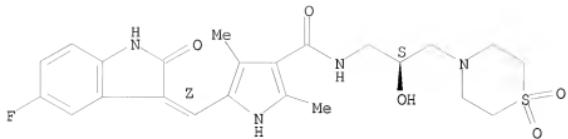


RN 452105-45-2 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[(2S)-3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

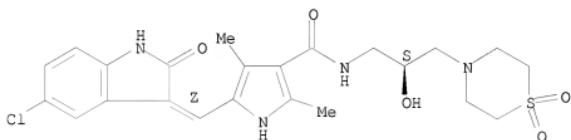


RN 452105-46-3 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-chloro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

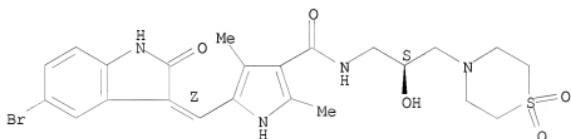


RN 452105-47-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

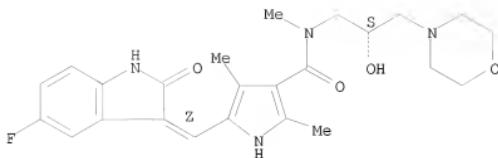


RN 452105-62-3 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2S)-2-hydroxy-3-(4-morpholinyl)propyl]-N,2,4-trimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

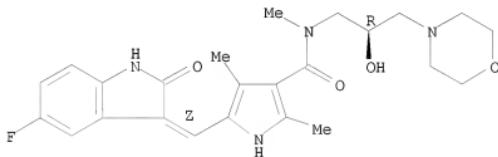


RN 452105-63-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[(2R)-2-hydroxy-3-(4-morpholinyl)propyl]-N,2,4-trimethyl- (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 8 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2002:539677 HCPLUS

DOCUMENT NUMBER: 137:109202

TITLE: Preparation of 4-aryl substituted indolinones as protein kinase signal transduction modulators for inhibiting abnormal cell proliferation

INVENTOR(S): Cui, Jingrong; Zhang, Ruofei; Shen, Hong; Chu, Ji Yu; Zhang, Fang-Jie; Koenig, Marcel; Do, Steven Huy; Li, Xiaoyuan; Wei, Chung Chen; Tang, Peng Cho

PATENT ASSIGNEE(S): USA

SOURCE: PCT Int. Appl., 560 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055517	A2	20020718	WO 2001-US48564	20011220 <--
WO 2002055517	A3	20020926		
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW	CA 2432114 A1 20020718 CA 2001-2432114 20011220 <--
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BE, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MC, NE, SN, TD, TG	AU 2002248186 A1 20020724 AU 2002-248186 20011220 <--
US 20030069297 A1 20030410 US 2001-23488 20011220 <--	US 6677368 B2 20040113
EP 1349852 A2 20031008 EP 2001-997065 20011220 <--	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2004518669 T 20040624 JP 2002-556186 20011220	JP 20040157909 A1 20040812 US 2003-736243 20031216
US 6861418 B2 20050301	US 2000-256479P P 20001220 US 2001-23488 A3 20011220 WO 2001-US48564 W 20011220
PRIORITY APPLN. INFO.:	MARPAT 137:109202
OTHER SOURCE(S):	GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [R1 = (un)substituted aryl or heteroaryl; R2 = H, halo, alkyl, alkenyl, alkynyl, heterocycl, etc.; R3 = (un)substituted pyrrole or cycloalkenylpyrrole], as well as pharmaceutical compns. thereof, are prepared and disclosed as compds. capable of modulating protein kinase signal transduction in order to regulate, modulate and/or inhibit abnormal cell proliferation. Thus II, was prepared via condensation of 4-phenyl-1,3-dihydroindol-2-one with 5-formyl-2-methyl-4-[3-(4-methylpiperazin-1-yl)propyl]-1H-pyrrole-3-carboxylic acid Et ester. I were evaluated against eight specific kinases, e.g., FGFR1, for which I possessed IC50 values ( $\mu$ M) of 0.0091-2.07. The present invention also relates to methods for treating protein kinase related disorders.

IT 442559-57-1P 442560-03-4P 442560-04-5P  
442560-39-6P 442560-83-0P 442561-11-7P  
442561-12-8P 442561-13-9P 442561-76-4P  
442561-77-5P

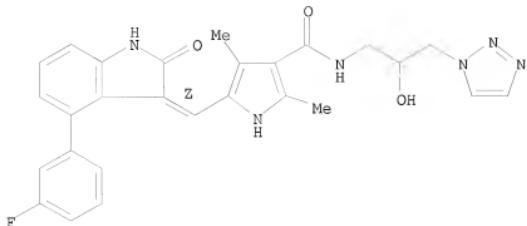
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of (aryl)(pyrrolylmethylene)indolinones as protein kinase signal transduction modulators)

RN 442559-57-1 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

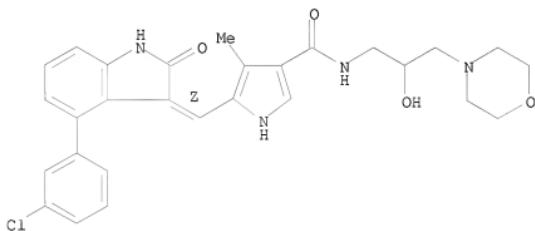
Double bond geometry as shown.



RN 442560-03-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(3-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(4-morpholinyl)propyl]-4-methyl- (CA INDEX NAME)

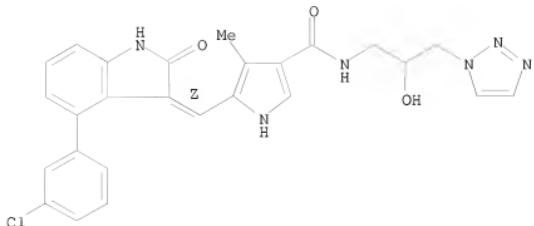
Double bond geometry as shown.



RN 442560-04-5 HCPLUS

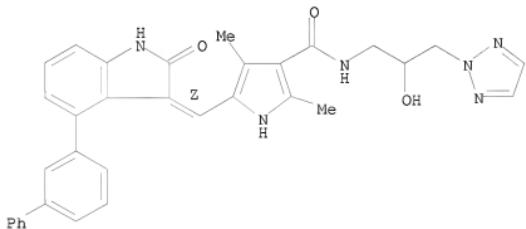
CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(3-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(1H-1,2,3-triazol-1-yl)propyl]-4-methyl- (CA INDEX NAME)

Double bond geometry as shown.



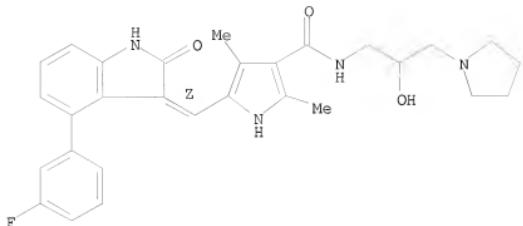
RN 442560-39-6 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(4-[1,1'-biphenyl]-3-yl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(2H-1,2,3-triazol-2-yl)propyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



RN 442560-83-0 HCPLUS  
 CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(4-(3-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[2-hydroxy-3-(1-pyrrolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

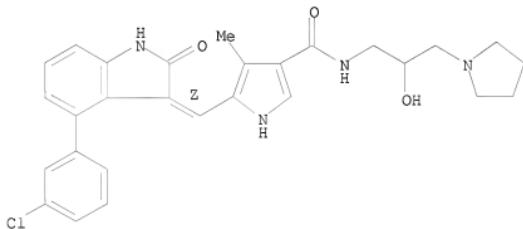
Double bond geometry as shown.



RN 442561-11-7 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-{4-(3-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene}methyl]-N-[2-hydroxy-3-(1-pyrrolidinyl)propyl]-4-methyl-  
(CA INDEX NAME)

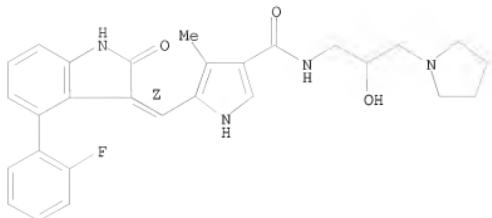
Double bond geometry as shown.



RN 442561-12-8 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-{4-(2-fluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene}methyl]-N-[2-hydroxy-3-(1-pyrrolidinyl)propyl]-4-methyl-  
(CA INDEX NAME)

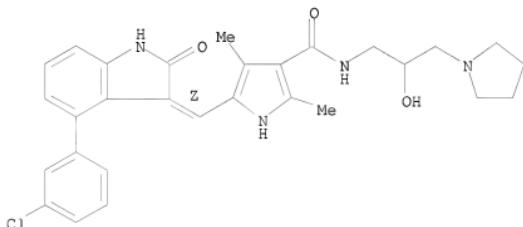
Double bond geometry as shown.



RN 442561-13-9 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(3-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[2-hydroxy-3-(1-pyrrolidinyl)propyl]-2,4-dimethyl- (CA INDEX NAME)

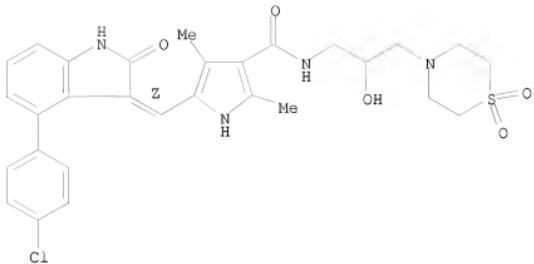
Double bond geometry as shown.



RN 442561-76-4 HCPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(4-chlorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene]methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-2,4-dimethyl- (CA INDEX NAME)

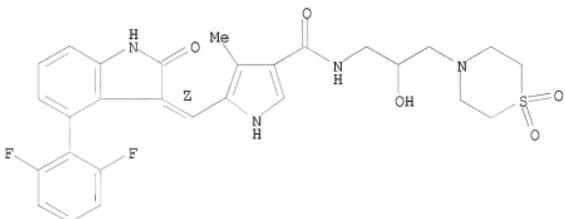
Double bond geometry as shown.



RN 442561-77-5 HCAPLUS

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-[4-(2,6-difluorophenyl)-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-N-[3-(1,1-dioxido-4-thiomorpholinyl)-2-hydroxypropyl]-4-methyl- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:868415 HCAPLUS

DOCUMENT NUMBER: 136:697

TITLE: Mannich base prodrugs of 3-(pyrrol-2-ylmethyldene)-2-indolinone derivatives

INVENTOR(S): Moon, Malcolm Wilson; Morozowich, Walter; Gao, Ping; Tang, Peng Cho

PATENT ASSIGNEE(S): Sugen, Inc., USA; Pharmacia &amp; Upjohn Company

SOURCE: PCT Int. Appl., 96 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090068	A2	20011129	WO 2001-US16757	20010524 <--
WO 2001090068	A3	20020606		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 270545	B	20070111	TW 2001-90112409	20010523
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AU 2001064885	A	20011203	AU 2001-64885	20010524 <--
US 20020032204	A1	20020314	US 2001-863804	20010524 <--
US 6710067	B2	20040323		
US 20020035140	A1	20020321	US 2001-863905	20010524 <--
US 6451838	B2	20020917		
US 20020037878	A1	20020328	US 2001-863819	20010524 <--
US 6482848	B2	20021119		
EP 1301507	A2	20030416	EP 2001-939357	20010524 <--
EP 1301507	B1	20060719		
R: AI, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003534323	T	20031118	JP 2001-586257	20010524 <--
ES 2253385	T3	20060601	ES 2001-937687	20010524
AT 333453	T	20060815	AT 2001-939357	20010524
ES 2269416	T3	20070401	ES 2001-939357	20010524
US 20030045565	A1	20030306	US 2002-243663	20020916 <--
US 20030083363	A1	20030501	US 2002-243942	20020916 <--
US 6716870	B2	20040406		
US 20040127542	A1	20040701	US 2003-429895	20030505
US 7008943	B2	20060307		
HK 1054552	A1	20061208	HK 2003-106800	20030922
US 20040127544	A1	20040701	US 2003-743909	20031224
US 7053113	B2	20060530		
US 20050107340	A1	20050519	US 2004-774415	20040210
US 7112603	B2	20060926		
PRIORITY APPLN. INFO.:				
		US 2000-207000P	P 20000524	
		US 2000-225045P	P 20000811	
		US 2001-863804	A1 20010524	
		US 2001-863819	A3 20010524	
		US 2001-863905	A1 20010524	
		WO 2001-US16757	W 20010524	
		US 2002-243663	B1 20020916	
		US 2002-243942	A1 20020916	

OTHER SOURCE(S): MARPAT 136:697

AB The present invention is directed to Mannich base prodrugs of certain 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs. that modulate the activity of protein kinases ("PKs"). Pharmaceutical compns. comprising these compds., methods of treating diseases related to abnormal PK activity utilizing pharmaceutical compns. comprising these compds. and methods of preparing them are also disclosed.

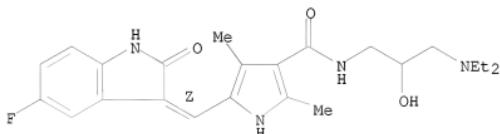
IT 375798-55-3P  
RL: SPN (Synthetic preparation); PREP (Preparation)

(Mannich base prodrugs of 3-(pyrrol-2-ylmethylidene)-2-indolinone derivs.)

RN 375798-55-3 HCPLUS

CN 1H-Pyrrole-3-carboxamide, N-[3-(diethylamino)-2-hydroxypropyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl- (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L21 HAS NO ANSWERS
'IBIB ABS ' IS NOT A VALID STRUCTURE FORMAT KEYWORD
Structure Formats
SIA ----- Structure Image, Attributes, and map table if it contains
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SIM ----- Structure IMage.
SAT ----- Structure ATtributes and map table if it contains data.
SCT ----- Structure Connection Table and map table if it contains
        data.
SDA ----- All Structure DAta (image, attributes, connection table and
        map table if it contains data).
NOS ----- NO Structure data.
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L8          46 S L7
L9          853 S L8 SSS FULL
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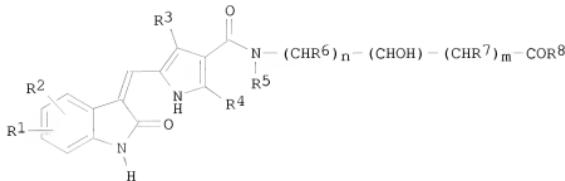
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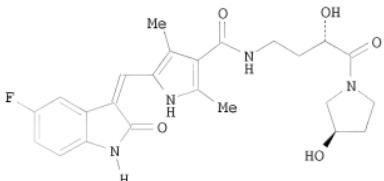
L19 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 20061342422 HCAPLUS  
 DOCUMENT NUMBER: 146:81764  
 TITLE: Enhanced indolinone based protein kinase inhibitors and their preparation, pharmaceutical compositions and use in the treatment of cancer  
 INVENTOR(S): Liang, Congxin; Feng, Yangbo; Vojkovsky, Tomas  
 PATENT ASSIGNEE(S): The Scripps Research Institute, USA  
 SOURCE: U.S. Pat. Appl. Publ., 78pp., Cont.-in-part of Appl. No. PCT/US2004/39725.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060287381	A1	20061221	US 2006-441537	20060526
WO 2005053686	A1	20050616	WO 2004-US39752	20041126
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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PRIORITY APPLN. INFO.:			WO 2004-US39752	A2 20041126
			US 2005-685144P	P 20050526
			US 2005-754360P	P 20051228
			US 2003-525430P	P 20031126
			US 2004-545721P	P 20040218

OTHER SOURCE(S): MARPAT 146:81764  
 GI



I



II

**AB** Hydroxy carboxy pyrrolyl-indolinone derivs. of formula I have enhanced and unexpected drug properties as inhibitors of protein kinases and are useful in treating disorders related to abnormal protein kinase activities such as cancer. More particularly, alpha-hydroxy-omega-(2-oxo-indolylidenemethyl-pyrrole-3'-carbonyl) amino alcanoic acid and amide derivs. have enhanced and unexpected drug properties as inhibitors of protein kinases with respect to their corresponding beta-hydroxy-omega-(2-oxo-indolylidenemethyl-pyrrole-3'-carbonyl) amino alcanoic acid and amide derivs. and are useful in treating disorders related to abnormal protein kinase activities such as cancer. Compound of formula I wherein R1 and R2 are independently H, halo, C1-6 (halo)alkyl, C3-8 cycloalkyl, OH, amino, etc.; R3 is H, C1-6 alkyl, C6-10 aryl, C5-10 heteroaryl, and amide; R3 - R6 are independently H and C1-6 alkyl; R7 is H, C1-6 alkyl, and OH; R8 is OH, C1-6 O-alkyl, C3-8 cycloalkyl and NH2 and derivs., etc.; n and m are independently 0, 1, 2, and 3; and their pharmaceutically acceptable salts, tautomers, and prodrugs thereof, are claimed. Example compound II was prepared by amidation of (S)-4-((15-[5-fluoro-2-oxo-1,2-dihydroindol-1(3Z)-ylidenemethyl]-2,4-dimethyl-1H-pyrrole-3-carbonyl)amino)-2-hydroxybutyric acid with (R)-3-hydroxypyrrolidine. All the invention compds. were evaluated for their protein kinase inhibitory activity. From the assay, it was determined that compound II exhibited and IC50 value of < 0.003  $\mu$ M.

L19 ANSWER 2 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2006:1252701 HCPLUS

DOCUMENT NUMBER: 146:27724

TITLE: Preparation of (pyrrolylmethylidene)indolinones as protein kinase inhibitors for the treatment of cancer

INVENTOR(S): Liang, Congxin; Feng, Yangbo; Vojkovsky, Tomas

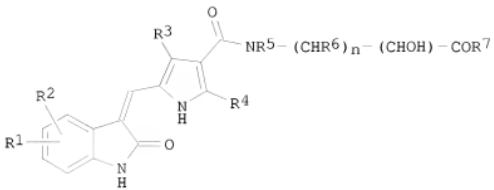
PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 49pp.

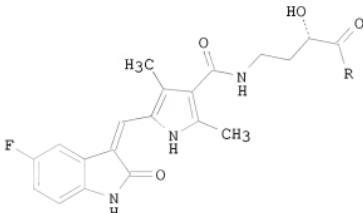
CODEN: PIXXD2  
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 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006127961	A1	20061130	WO 2006-US20363	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
AU 2006249790	A1	20061130	AU 2006-249790	20060526
CA 2610067	A1	20061130	CA 2006-2610067	20060526
EP 1893194	A1	20080305	EP 2006-771248	20060526
R: AI, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
JP 2008542294	T	20081127	JP 2008-513740	20060526
MX 2007014810	A	20080221	MX 2007-14810	20071126
IN 2007DΝ09747	A	20080620	IN 2007-DΝ5747	20071217
KR 2008017058	A	20080225	KR 2007-730412	20071226
CN 101222920	A	20080716	CN 2006-80025908	20080115
PRIORITY APPLN. INFO.:			US 2005-685144P	P 20050526
			US 2005-754360P	P 20051228
			WO 2006-US20363	W 20060526

OTHER SOURCE(S): CASREACT 146:27724; MARPAT 146:27724  
 GI



I



II

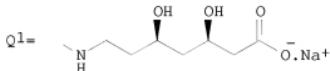
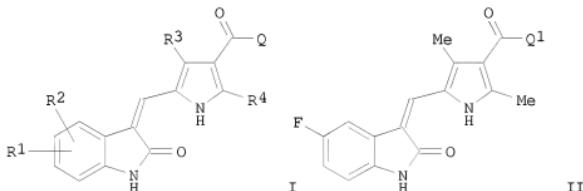
**AB**  $\alpha$ -Hydroxy- $\omega$ -[5-(2-oxo-indol-3-ylidenemethyl)pyrrol-3-ylcarbonylamino]alkanoic acids and their derivs. I [wherein R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl, (hetero)aryl or amide; R4 - R6 = H or alkyl; R7 = OH, O-(alkyl), O-(cyclo)alkyl or (un)substituted amino; n = 1-3] and pharmaceutically acceptable salts, tautomers and prodrugs thereof were prepared as protein kinase inhibitors. For instance, II (R = OH) was synthesized via successive treatment of the corresponding pyrrolecarboxylic acid with HATU, amidation of the resultant active ester with Me (2S)-4-amino-2-hydroxybutyrate hydrochloride, and ester hydrolysis. Further amidation of acid II (R = OH) with amines led to a number of amides, such as III (R = NMe<sub>2</sub>, III). III had an IC<sub>50</sub> of < 0.003  $\mu$ M against KDR in VEGFR biochemical assay. Therefore, the invented compds. are useful in treating disorders related to abnormal protein kinase activities such as cancer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN  
 ACCESSION NUMBER: 2005:523281 HCPLUS  
 DOCUMENT NUMBER: 143:59818  
 TITLE: Preparation of 2-[(2-oxo-1,2-dihydro-indol-3-ylidene)methyl]pyrrole-4-carboxamide derivatives as protein kinase inhibitors  
 INVENTOR(S): Liang, Congxin  
 PATENT ASSIGNEE(S): The Scripps Research Institute, USA  
 SOURCE: PCT Int. Appl., 54 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

OTHER SOURCE(S): CASREACT 143:59818; MARPAT 143:59818  
GI



AB The title compds. (I) [wherein R1 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, Cl-6 alkoxy, NH2, Cl-6 alkylamino, amide, sulfonamide, cyano, (un)substituted C6-10 aryl; R2 = H, halo, C1-6 alkyl, C3-8 cycloalkyl, C1-6 haloalkyl, HO, Cl-6 alkoxy, C2-8 alkoxyalkyl, NH2, Cl-6 alkylamino, C6-10 arylamino; R3 = H, Cl-6 alkyl, C6-10 aryl, C5-10

heteroaryl, amide; R4-R6 = H, C1-6 alkyl; R7 = H, C1-6 alkyl, HO; R8 = HO, C1-6 alkoxy, C3-8 cycloalkoxy, NR9R10 (where R9, R10 = H, C1-6 alkyl, C1-6 hydroxyalkyl, C1-6 dihydroxyalkyl, C1-6 alkoxy, C1-6 alkylcarboxylic acid, C1-6 alkylphosphoric acid, C1-6 alkylsulfuric acid, C1-6 hydroxyalkylcarboxylic acid, C1-6 alkyl amide, C3-8 cycloalkyl, C5-8 heterocycloalkyl, C6-8 aryl, C5-8 heteroaryl, C3-8 cycloalkylcarboxylic acid; or NR9R10 together forms (un)substituted (C5-C8) heterocyclic); n, m = 0-3; p = 1-3] or pharmaceutically acceptable salts, their tautomers, pharmaceutically acceptable salts of their tautomer, or prodrugs thereof are prepared. These compds. have enhanced and unexpected drug properties as inhibitors of protein kinases, in particular VEGF receptors and PDGF receptors, and are useful in treating disorders related to abnormal protein kinase activities such as cancer (no data). Thus, 5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid was condensed with (4R,6R)-[6-(2-aminoethyl)-2,2-dimethyl-1,3-dioxan-4-yl]acetic acid tert-Bu ester using 3-dimethylaminopropyl-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole in DMF at room temperature for 30 h followed by treatment with a mixture of 2 N aqueous HCl, THF, and EtOH, neutralization with aqueous NaHCO<sub>3</sub>, extraction with Me tert-Bu ether to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxyl]amino]-3,5-dihydroxyheptanoic acid tert-Bu ester which was stirred with a mixture of aqueous NaOH solution and MeOH at room temperature for 3 h to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxyl]amino]-3,5-dihydroxyheptanoic acid sodium salt (II).

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 4 HCPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2005:523237 HCPLUS

DOCUMENT NUMBER: 143:59816

TITLE: Preparation of advanced indolinone based protein kinase inhibitors

INVENTOR(S): Liang, Congxin

PATENT ASSIGNEE(S): The Scripps Research Institute, USA

SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

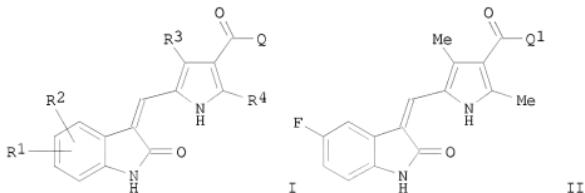
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

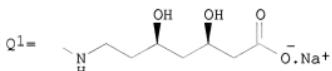
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005053614	A2	20050616	WO 2004-US39728	20041126
WO 2005053614	A3	20060223		
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO,			

SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004294981	A1	20050616	AU 2004-294981	20041126
CA 2547066	A1	20050616	CA 2004-2547066	20041126
EP 1686987	A2	20060809	EP 2004-812287	20041126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
CN 1905869	A	20070131	CN 2004-80040854	20041126
BR 2004016994	A	20070206	BR 2004-16994	20041126
JP 2007512353	T	20070517	JP 2006-541462	20041126
MX 20060606049	A	20070524	MX 2006-6049	20060526
IN 2006DN03108	A	20070824	IN 2006-DN3108	20060531
US 20080044881	A1	20080221	US 2007-580670	20070412
PRIORITY APPLN. INFO.:			US 2003-525430P	P 20031126
			US 2004-545721P	P 20040218
			WO 2004-US39728	W 20041126

OTHER SOURCE(S): CASREACT 143:59816; MARPAT 143:59816  
GI



$$Q = -NR^6 - (CHR^6)_n - [CH(OH) - (CHR^7)_m]_p - COR^8$$



C5-8 heteroaryl, C3-8 cycloalkylcarboxylic acid; or NR9R10 together forms (un)substituted (C5-C8) heterocyclic; n, m = 0-3; p = 1-3] or pharmaceutically acceptable salts, their tautomers, pharmaceutically acceptable salts of their tautomer, or prodrugs thereof are prepared. These compds. have enhanced and unexpected drug properties as inhibitors of protein kinases, in particular VEGF receptors and PDGF receptors, and are useful in treating disorders related to abnormal protein kinase activities such as cancer (no data). Thus, 5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid was condensed with (4R,6R)-[6-(2-aminoethyl)-2,2-dimethyl-1[1,3]dioxan-4-yl]acetic acid tert-Bu ester using 3-dimethylaminopropyl-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole in DMF at room temperature for 30 h followed by treatment with a mixture of 2 N aqueous HCl, THF, and EtOH, neutralization with aqueous NaHCO<sub>3</sub>, extraction with Me tert-Bu ether to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carbonyl]amino]-3,5-dihydroxyheptanoic acid tert-Bu ester which was stirred with a mixture of aqueous NaOH solution and MeOH at room temperature for 3 h to give (3R,5R)-7-[5-(5-fluoro-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carbonyl]amino]-3,5-dihydroxyheptanoic acid sodium salt (II).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FULL ESTIMATED COST		ENTRY	SESSION
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)		SINCE FILE	TOTAL
CA SUBSCRIBER PRICE		ENTRY	SESSION
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STN INTERNATIONAL LOGOFF AT 11:45:19 ON 13 JUL 2009